IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

NATERA, INC.,	)	
	)	C.A. No. 20-125 (LPS)
Plaintiff,	)	(CONSOLIDATED)
	)	
v.	)	**JURY TRIAL DEMANDED**
	)	
ARCHERDX, INC., ARCHERDX, LLC and INVITAE CORP.,	)	**REDACTED – PUBLIC VERSION**
	)	
Defendants.	)	

NATERA'S OPPOSITION TO DEFENDANTS' MOTION FOR SUMMARY JUDGMENT AND TO EXCLUDE EXPERT TESTIMONY

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Original Filing Date: February 11, 2022
Redacted Filing Date: February 21, 2022

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I. INTRODUCTION

Defendants ArcherDX, Inc., ArcherDX, LLC and Invitae Corp.'s (collectively "Defendants") motion for summary judgment and to exclude testimony is unwarranted. The asserted summary judgment grounds are rife with factual disputes, untethered to the court's construction, and cannot sustain Defendants' heavy burden of proving invalidity. The motion to exclude expert testimony is based on selective "facts" taken out of context, misquoted opinions, and misapplication of the Court's claim construction. Defendants' motion should be denied.[1]

II. ARGUMENT

A. MATERIAL ISSUES OF FACT PRECLUDE SUMMARY JUDGMENT OF NON-INFRINGEMENT OF THE ASSERTED '482, '172 AND '814 PATENT CLAIMS

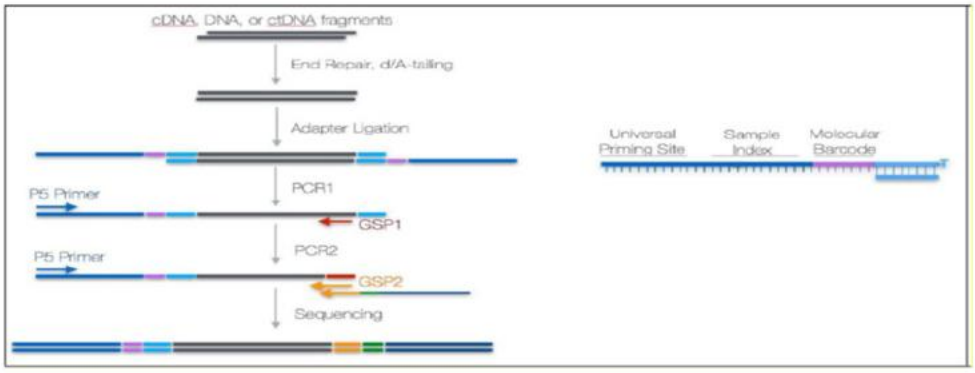
1. The Claimed "Universal Primer" Is Literally Present in the Accused Products

The factual dispute over whether "the universal primer" limitation, recited in all asserted claims of the '482, '172, and '814 patents, is literally present in the accused products alone precludes summary judgment. The accused products use the "P5_1" primer consisting of 26 nucleotides as a universal primer in the first PCR reaction. Ex. 15, Cooper NI Rpt. ¶ 43. The accused products use the "P5_2" primer with the exact same 26-nucleotide universal priming sequence, plus three additional nucleotides on one end, in the second PCR reaction. *Id*. Thus, the same 26-nucleotide "universal primer" present in the first PCR reaction is also present in the second PCR reaction in the accused products, as required by the claims. Ex. 18, Quackenbush Reply Rpt. ¶¶ 31-33. As such, the accused products literally meet "the universal primer" claim limitation.

Defendants admitted as much in submissions to the FDA. In their Premarket Application

[1] The pertinent facts are included in opposition to each ground of summary judgment.

to the FDA, Defendants identify the universal primer as the same "P5 primer" in the "first" PCR (PCR1) and "second" PCR (PCR2) steps of the accused products, as depicted below:



Ex. 1, [redacted], ARCHER00044976 atARCHER00044991. This is undisputed. Defendants would not have made this representation to the FDA, knowing that the FDA requires the applicant to provide accurate information, if they did not believe that the same universal P5 primers are used in the two PCR steps.

At a minimum, Defendants' argument that the universal primers in the two PCR reactions are different—despite having the exact same 26-nucleotide priming sequence—creates a disputed issue of material fact unsuited for resolution on summary judgment, particularly in view of their representations to the FDA to the contrary. (*See* Ex. 13, Quackenbush Opening Rpt. ¶¶ 266-268, Ex. 18, Quackenbush Reply Rpt. ¶¶ 31-33, Ex. 15, Cooper Rebuttal NI Rpt. ¶¶ 73-75). *Reeves v. Sanderson Plumbing Prods., Inc.*, 530 U.S. 133, 150 (2000) (The Court must "draw all reasonable inferences in favor of the nonmoving party, and it may not make credibility determinations or weigh the evidence."). A jury should weigh Defendants' litigation contentions against their representations to the FDA and the undisputed evidence that the universal primer used in the first PCR step is also fully used in the second step.

2. The Disclosure-Dedication Rule Is Inapplicable Because the Subject Matter at Issue Is Not Unclaimed and the Alleged Disclosure Does Not Amount to a Specific, Unclaimed Alternative

Even if the claimed "the universal primer" limitation were not literally present, it is met under the doctrine of equivalents. Defendants argue that the disclosure in the patent specifications about the use of different universal primers in successive PCR steps precludes the application of doctrine of equivalents. Br. at 5-6. This argument lacks merit.

First, as discussed above, this is not a situation involving an unclaimed embodiment—a second universal primer having an identical universal priming sequence as the first universal primer plus a few *additional* nucleotides is still covered by the claims. Thus, the patentee in fact claimed this subject matter and did not dedicate it to the public.[2] *Guardant Health, Inc. v. Found. Med., Inc.*, Nos. 17-1616 & 17-1623, D.I. 437 at *24 (D. Del. May 7, 2020) ("The disclosure-dedication rule is only triggered when the patentee 'declines to claim subject matter' that is disclosed in the written description.") adopted in D. Del. Oct. 9, 2020 ruling, D.I. 482; *Eli Lilly & Co. v. Hospira, Inc.*, 933 F.3d 1320, 1334 (Fed. Cir. 2019) ("The reason for the doctrine is that members of the public reading a disclosure of particular subject matter are entitled, absent a claim to it, to assume that it is not patented and therefore dedicated to the public (unless, for example, claimed in a continuation or other application based on the disclosure.");[3] *see also Viiv Healthcare*

[2] Indeed, Defendants do not dispute that the supposedly unclaimed second universal primer is expressly claimed in the related '220 patent, which rebuts an inference of dedication. *Guardant Health, Inc. v. Foundation Medicine, Inc.*, Nos. 17-1616 & 17-1623, D.I. 437 at *24 (D. Del. May 7, 2020) (Dedication-disclosure rule is not a legal bar "because, for example, claim 13 of the '992 Patent (a continuation-in-part of the '731 patent) recites elimination of some parent polynucleotides prior to the sequencing step."); *Eli Lilly & Co. v. Hospira, Inc.*, 933 F.3d at 1334.

[3] The cases Defendants cite for the proposition "later-filed patent reinforces that the disclosure-dedication rule applies to its earlier patents," Br. 6-7, are not so expansive, and further were decided ***before*** the *Lilly* decision. In *CSP Techs., Inc. v. Sud-Chemie AG*, the Court stated that a later filed application "reinforces our view that the ***district court appropriately applied*** the disclosure-dedication doctrine," not that later filed applications *per se* support a finding of disclosure-dedication. 643 F. App'x 953, 958 (Fed. Cir. 2016) (emphasis added). Likewise, *In re Bendamustine Consol. Cases*, is consistent with the idea that later filed applications do not necessarily support a finding of disclosure-dedication. No. CV 13-2046-GMS, 2015 WL 1951399,

Co. v. Gilead Scis., Inc., No. 18-224-CFC, 2020 WL 567398, at *3 (D. Del. Feb. 5, 2020).

Second, Defendants' arguments fail because the disclosure-dedication rule only applies to embodiments that are clearly disclosed as an ***alternative*** to the claimed subject matter but left unclaimed. This is not true here. *Eli Lilly* is illustrative. In *Eli Lilly*, the claim was to administration of pemetrexed ***disodium*** (a type of antifolate) and the alleged alternative was administration of pemetrexed ***ditromethamine***. 933 F.3d at 1325, 1334. The patent listed pemetrexed disodium as the most preferred antifolate, "as well as 'derivatives described in' several patents including the Akimoto patent" as preferred antifolates. *Id*. at 1325. DRL contended that pemetrexed ***ditromethamine*** was one of the derivatives taught in the Akimoto patent, but not claimed by Lilly and therefore dedicated to the public. *Id*. at 1334. Rejecting DRL's disclosure argument, the Court explained: the formula disclosed in Akimoto "encompasses thousands of compounds," tromethamine is not expressly disclosed "but only generically among dozens of other salts," and "[a]t most, Akimoto discloses ammonium salts generally, which is far from a description of tromethamine." *Id*. at 1335. The Court concluded, "Akimoto contains only a 'generic reference' to premetrexed ditromethamine" and "it was not dedicated to the public." *Id*.

Here too, as in *Lilly*, the patents generically describe universal primers. From this generic disclosure a skilled artisan would not identify that a second universal primer having an identical universal priming sequence as the first universal primer ***plus three extra nucleotides*** has been disclosed as an ***alternative*** to a second universal primer consisting only the sequence of the first universal primer. "The disclosure must be clear and precise." *Sun Pharm Indus. Ltd. v Saptalis Pharms., LLC*, NO. 18-cv-648, D.I. 146, at *22 (D. Del. Aug. 19, 2019) ("Merely disclosing, in

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at *3 (D. Del. Apr. 29, 2015). *ViiV Healthcare UK Ltd. v. Lupin Ltd*., does not even address the disclosure-dedication doctrine. 6 F. Supp. 3d 461, 473 (D. Del. 2013).

generic terms, alternative formulations that contain a sweetener and a taste-masking agent, but that exclude polyhydroxy alcohol, does not amount to the dedication of all metformin formulations containing a sweetener and a taste-masking agent other than a polyhydroxy alcohol"); *SanDisk Corp. v. Kingston Tech. Co., Inc.,* 695 F.3d 1348, 1363 (Fed. Cir. 2012) (The disclosure-dedication does not encompass any "generic reference" in a written specification; "disclosure must be of such specificity that one of ordinary skill in the art could identify the subject matter that had been disclosed and not claimed."); *Pfizer, Inc. v. Teva Pharms. USA, Inc.,* 429 F.3d 1364, 1379 (Fed. Cir. 2005) (the "unclaimed subject matter must have been identified by the patentee as an alternative to a claim limitation.").

Defendants do not identify anything in the specification but generically assert that the patents disclose "different" universal primers in successive PCR steps (Br. at 6),[4] and contend that these allegedly "different" universal primers have been dedicated to the public. That generic disclosure is insufficient to trigger the disclosure-dedication rule. *See F'Real Foods, LLC v. Hamilton Beach Brands, Inc.*, NO. 16-cv-41, 2020 WL 2085692, at *2 (D. Del. Apr. 30, 2020) ("a generic disclosure to the use of a 'weight to hold the shield and cup in place' does not dedicate all uses of weights to the public.").

Third, the difference between the sequences of P5_1 and P5_2 universal primers is so

[4] The specification cites identified by Defendants' expert underscores the genericness of the disclosure. Some of the cites do not mention universal primers (D.I. 433-1, Ex. 1, '814 Patent, 37:57; 7:17-26; Ex. 15, Cooper NI Rpt. ¶¶ 76, 78). Other cites describe PCR workflows which utilize universal primers (Ex. 15, Cooper NI Rpt. ¶ 81), but they do not disclose a second universal primer having an identical universal priming sequence as the first universal primer plus three extra nucleotides as an ***alternative*** to a second universal primer having the sequence of the first universal primer. Likewise, Defendants' reference to Natera's expert testimony about disclosure of different universal primers (Br. at 6) does not support that the patentee dedicated a second universal primer having an identical universal priming sequence as the first universal primer ***plus three extra nucleotides*** to the public. Rather, his opinion that the accused products literally meet the claim limitation indicates the opposite—the patentee claimed such universal primers.

trivial that this is precisely the type of situation for which doctrine of equivalents should be made available: to prevent "the unscrupulous copyist [from] mak[ing] unimportant and insubstantial changes and substitutions in the patent which, though adding nothing, would be enough to take the copied matter outside the claim, and hence outside the reach of law." *Graver Tank & Mfg. Co. v. Linde Air Prods. Co*., 339 U.S. 605, 607 (1950).

Summary judgment of non-infringement of the asserted '482, '172 and '814 patent claims should be denied.

B. FACT DISPUTES PRECLUDE SUMMARY JUDGMENT OF NON-INFRINGEMENT OF THE '708 PATENT

Genuine issues of material facts over whether the accused products read on claims 1, 9, and 19 of the '708 Patent ("the Asserted '708 Claims") preclude summary judgment. Specifically, the parties have a factual dispute over the correct application of the Court's construction of the claim terms (1) "at least 2 primers," and (2) "melting temperature," and (3) over whether Defendants' contemporaneous technical documents show the claimed "melting temperatures" of the primers used in the accused products. Summary judgment is unwarranted. *Edwards Sys. Tech., Inc. v. Digital Control Sys., Inc.*, 99 F. App'x 911, 922 (Fed. Cir. 2004) ("This conflicting evidence demonstrates a classic battle of the experts as to whether [the accused products meet the claim limitation] and thus creates a genuine issue of material fact as to infringement of this limitation.")

The Asserted '708 Claims require "the annealing temperature for the reaction conditions [be] greater than a melting temperature of the at least 2 primers…" D.I. 433-2, '708 Patent, cl. 1. The Court construed "a melting temperature of the at least 2 primers" to mean "the temperature at which one-half (50%) of a DNA duplex of each primer and its perfect complement dissociates and becomes single-strand DNA" and explained, "when multiple primers are involved, an annealing temperature that is ***greater than*** 'a melting temperature of the at least 2 primers' is one that is

higher than each individual melting temperature of each primer." D.I. 243 at 10-11 (emphasis in original).

Natera's expert Dr. Quackenbush correctly applied the Court's construction in his infringement analysis to show that for each of the accused products, the annealing temperature for the PCR reaction conditions is greater than ***each of the melting temperatures of at least 2 of the primers***. Ex. 13, Quackenbush Rpt. ¶¶ 367-382, Ex. 18, Quackenbush Reply Rpt. ¶¶ 52-54. Defendants however, argue that to infringe, not just "at least 2 primers"—such as six primers—but ***every*** primer in the accused product (for VariantPlex CTL, all 628 primers) must each have a melting temperature that is less than the annealing temperature. Br. 7-8. Defendants' reading nullifies the claim language "at least 2" from "at least 2 primers." Defendants misconstrue the Court's construction explaining that "'***a***' melting temperature of two or more primers is not ***one*** measurement that relates to the whole of all the primers collectively, but instead refers to the specific melting temperature for each of the primers." D.I. 243 at 11 (emphasis added). That is, the claim, which requires "at least 2 primers," is infringed so long as the annealing temperature is higher than the melting temperature of each of any two primers present in the reaction, regardless of whether additional primers are present. It does not require that the annealing temperature be higher than the melting temperature of ***every*** primer in the reaction. Summary judgment of non-infringement is inappropriate.

Dr. Quackenbush correctly applied the Court's construction of "melting temperature" to the ***complementary*** segment of the primers used in the accused products. Ex. 13, Quackenbush Rpt. ¶¶ 367-382, Ex. 18, Quackenbush Reply Rpt. ¶¶ 55-57. Per the Court's construction, "melting temperature" is the temperature at which one-half of a "***DNA duplex of each primer and its perfect complement dissociates*** and becomes single strand DNA." D.I. 243 at 10 (emphasis added). It is

undisputed that the primers in the accused products include a segment complementary to the target sequence ("complementary segment") and a segment not complementary to the target sequence ("tail segment"). Br. 8. Thus, the phrase "DNA duplex of each primer and its perfect complement" refers to the ***complementary segment*** of the primer and its perfect complement (the target sequence). Ex. 18, Quackenbush Reply Rpt. ¶ 55. The tail segment of the primer is ***not*** complementary, *i.e.*, it does not bind the target sequence and does not form a DNA duplex.

Defendants, however, contend that both the complementary and tail segments should be included in determining the melting temperature. Br. 8. According to Defendants, the term "primer" can include tail sequence and therefore the tail sequence should also be included in calculating primer melting temperature. Br. 8-10. But Defendants' argument flies in the face of the Court's construction that melting temperature is the temperature at which 50% of the "DNA duplex of each primer and its perfect complement dissociates." As stated above, the tail does not bind and does not form part of the duplex that the Courts construction requires.[5] These factual issue and disputes preclude summary judgment.

Defendants' own documents, which listed the melting temperatures of the primers used in the accused products, prove that the primer melting temperature limitation is met in the accused products. Ex. 13, Quackenbush Rpt. ¶¶ 367-382, Ex. 18, Quackenbush Reply Rpt. ¶ 54. Defendants argue that Dr. Quackenbush should not have relied on Defendants' documents, but instead should have performed his own calculations of primer melting temperature, purportedly because Dr. Quackenbush did not know how the melting temperatures in Defendants' documents were determined. Defendants argue that to read on the accused products, primer melting

[5] Tellingly, Defendants take the opposite tack to show invalidity—they rely only on the complementary segment of the primer to show that the primer melting temperature requirement is allegedly taught in prior art. Ex. 11, Cooper Rpt. ¶ 747.

temperature must be determined using the methods taught in the '708 Patent. Br. 11. Contrary to Defendants' contentions, Dr. Quackenbush properly relied on Defendants' documents to show infringement. Defendants do not dispute the accuracy of the documents. Defendants' Rule 30(b)(6) witness Ryan Walters testified that Primer3, one of the methods taught in the '708 Patent, could have been used to calculate the melting temperature of primers in the documents and that it was "a pretty common one." Ex. 4, Walters Tr. 135:21-136:7. Thus, it is more likely than not that the melting temperatures of the primers in these documents were computed using Primer3. Any doubt on how these melting temperatures in the documents were determined could have been settled by Defendants—after all, they are Defendants' documents. But Defendants adduce no evidence that a technique other than Primer3 were used to calculate the melting temperature identified in these documents. The reasonable inference in view of Defendants' silence is that the common Primer3 method was employed. And in any event, they have not shown that their own measurements are so erroneous that they engender any doubt as to the accuracy of their melting temperatures. These are issues for a jury to weigh.[6] This is a dispute over the weight of infringement evidence.

C. DEFENDANTS' NON-INFRINGEMENT ARGUMENT FOR LIQUIDPLEX, PCM AND STRATAFIDE FAILS AS A MATTER OF LAW

Defendants' non-infringement argument relies on a new claim construction position expressly contradicted by the Court's construction of "target loci" and therefore fails as a matter of law. Defendants contend that the accused products LiquidPlex, PCM and Stratafide cannot

[6] Moreover, Defendants should not be allowed to argue that Natera's expert should have performed the calculations (Br. 11) when Defendants withheld information on the reaction condition inputs required to calculate melting temperatures using Primer3. *See* Ex. 18, Quackenbush Reply Rpt. ¶ 59. Tellingly, for purposes of Defendants' prior art invalidity argument, their expert also did not calculate melting temperature of primers used allegedly in prior art, nor did he know how the primer melting temperatures were calculated. Ex. 7, Cooper (Vol. 2) Tr. 375:4-375:24.

infringe because they allegedly involve analysis of DNA from two individuals, circulating tumor DNA (the first individual) and circulating non-tumor DNA (the second individual), and the Court's construction of "target loci" supposedly requires the analysis of only one individual. Br. 13.

The Court's construction of "target loci," however, expressly includes scenarios where multiple DNA sources are present and the circulating tumor DNA is selected as target.

> "It may be that a single biological sample may contain material from multiple individuals. It may be possible, nonetheless, to practice the claims on such a sample, provided that each time it is practiced all of the target loci are selected from a single individual (i.e., the portion of the sample that is derived from that same single individual). For example, an individual looking to test for Y chromosome linked disorders could obtain a sample of mixed DNA from a mother and a fetus, target DNA of the fetus, and ***practice the claim with respect to the target loci of that fetus despite the presence of multiple DNA sources in the sample***. (Tr. at 27-28) ***The Court's construction is not intended to exclude such possibilities.***"

D.I. 243, n.3 (emphasis added). In fact, Defendants so argued during the *Markman* hearing: "just because you have a mixed sample that includes DNA from multiple individuals doesn't mean you can't target DNA from just one individual. You surely can. I just gave you an example of what you could do.") D.I. 185 at 27:20-24.[7] The accused products target tumor DNA. It does not matter whether circulating non-tumor DNA is present or not. Summary judgment is unwarranted.

D. THERE IS A GENUINE DISPUTE OF FACT OVER WHETHER BLOMQUIST ANTICIPATES OR RENDERS OBVIOUS THE ASSERTED '708 CLAIMS

1. Blomquist Does Not Anticipate the Asserted '708 Claims

Defendants have failed to show that Blomquist anticipates the asserted claims 1, 9 and 19

[7] Defendants' reference to Natera's experts' testimonies on the term "individual" (Br. 12-13) has no bearing here. Their testimonies were a response to Defendants' counsel's questions about a patent not at issue in this case. The term "individual" is ***not recited*** in the Asserted Claims, and Defendants wrongly imply that Natera's experts have construed the term "individual," when in fact Dr. Spellman candidly admitted that he had not reviewed the patent specification and testified to his understanding of the term in that limited context (Ex. 3, Spellman Tr. 50:11-51:9) and Dr. Quackenbush testified that the claims "haven't gone through a claim construction in this patent" (Ex. 6, Quackenbush Tr. 55:11-13).

of the '708 Patent. The clear and convincing evidentiary burden is particularly high on a motion for summary judgment where the evidence is construed in favor of the nonmovant. *United Access Techs., LLC v. AT&T Corp., et al*., 11-cv-339 (KAJ), 2021 WL 1840785, at *7 (D. Del. Apr. 30, 2021). Anticipation is a question of fact and "thus within the ordinary provenance of the jury." *Biogen MA Inv. v. EMD Serono, Inc.*, 976 F.3d 1326, 1332 (Fed. Cir. 2020). "A claim is anticipated only if each and every limitation is found within a single prior art reference." *Biogen MA Inv. v. EMD Serono, Inc.*, 976 F.3d 1326, 1331 (Fed. Cir. 2020).

Blomquist does not anticipate the Asserted '708 Claims because it at least does not teach the claim limitation "the annealing temperature for the reaction conditions is greater than a melting temperature of the at least 2 primers" recited in all three asserted claims. Ex. 16, Spellman Rpt. ¶¶ 73-78, 89-91. As Natera's expert Dr. Spillman explained, Blomquist does not disclose let alone teach an annealing temperature for the "primer extension reaction conditions" that is greater than the primer melting temperature. *Id*. Instead, Blomquist teaches that the annealing temperature varies from 72°C to 64°C in a single multiplex PCR reaction (with the annealing temperature decreasing by 1°C for every 5 cycles). The disclosed melting temperature of the primers is 68°C. Thus, the annealing temperature disclosed in Blomquist is ***not*** greater than the melting temperature of the primers "for the reaction conditions" (*i.e.*, when the annealing temperature is at 68°C or less); this is only true for ***a subset*** of the reaction conditions (*i.e.*, when the annealing temperature is at 69°C or higher). Ex. 16, Spellman Rpt. ¶ 89.[8]

[8] Defendants cast aspersions that Dr. Spellman "presented hardly any response" citing only ¶¶ 89-91 of Dr. Spellman's report (Br. 14). Contrary to Defendants' assertion, Dr. Spellman provided detailed opinions on Blomquist, including an overview of the reference and missing claim limitations in ¶¶ 73-78, opining on lack of anticipation in ¶¶ 89-91 and opining on non-obviousness in ¶¶ 178-187. *See* Ex. 16. A lawyer's characterization of an opinion as "hardly any response" does not negate the substance of the opinion for purposes of summary judgment.

Defendants do not dispute that the annealing temperature is not greater than primer melting temperature when the annealing temperature is at 68ºC or less, but argue that the claims do not require "the annealing temperature [to] exceed the melting temperature throughout an ***entire*** PCR protocol" and the claim limitation is met as long as the annealing temperature exceeds the primer melting temperature in some cycles of the reaction. Br. 14-15 (emphasis in original). Defendants' argument has no basis in claim language. Br. 14-15. The claim recites "primer extension reaction conditions" "wherein the annealing temperature ***for the reaction conditions*** is greater than a melting temperature." Nothing in this language suggests that annealing temperature can vary during the reaction conditions or that the claim is met even if the requisite temperature relationship holds for only a ***portion*** of the recited "reaction conditions," as Defendants posit. Contrary to Defendants' focus on the claim term "comprising" (Br. 15), while '"'comprising' 'permit[s] additional elements not required by a claim,' [] it 'does not remove the limitations that are present.'" *Guardant Health, Inc. v. Found. Med., Inc.*, No. CV 17-1616-LPS-CJB, 2020 WL 1329513, at *4 (D. Del. Mar. 23, 2020) (quoting *Power Mosfet Techs., L.L.C. v. Siemens AG*, 378 F.3d 1396, 1409 (Fed. Cir. 2004)). There is a factual dispute over whether clearly and indisputably teaches this claim limitation.[9]

2. Blomquist Does Not Render the Asserted '708 Claims Obvious

Through their expert, Defendants identified two references that, in combination with Blomquist, allegedly render the Asserted '708 Claims obvious. However, as Dr. Spellman explained, neither of these two references discloses the claim limitation missing in Blomquist, namely, "the annealing temperature for the reaction conditions is greater than a melting

[9] For a prior art reference to anticipate, it must also enable. *Am. Calcar, Inc. v. Am. Honda Motor Corp.*, 651 F.3d 1318, 1341 (Fed. Cir. 2011). As Dr. Spellman explained, Blomquist does not enable the Asserted '708 Claims because it teaches a different method—it teaches to change the annealing temperature during a single reaction. Ex. 16, Spellman Rpt. ¶ 90.

temperature of the at least 2 primers." Their combination with Blomquist therefore cannot, and does not, make the claims clearly and convincingly obvious. Ex. 16, Spellman Rpt., ¶¶ 73-78, 178-187. Defendants do not rebut Dr. Spellman's opinions or even address the alleged combination references in their motion.[10]

Taken together, "the evidence is such that a reasonable jury could return a verdict for" Natera that Blomquist neither anticipates nor renders obvious the Asserted '708 Claims. *Anderson v. Liberty Lobby, Inc*., 477 U.S. 242, 247-78 (1986). Summary judgment is unwarranted.

E. THE ASSERTED '708 PATENT CLAIMS ARE NOT INDEFINITE

Defendants repeat the same indefiniteness arguments they made and lost during the claim construction process and adduce no additional relevant evidence not already considered and found insufficient by the Court. D.I. 243 at 10, 12. Despite the Court expressly stating that the patent "contains guideposts for the POSA" and "the specification expressly discloses two measurement tools: ultraviolet light or Primer3/SantaLucia software" (D.I. 243 at 12), Defendants retread the same assertions: the patent does not specify a particular measurement method, Natera used an undisclosed method to compute melting temperature during the prosecution of a different patent, the two disclosed methods yield different results and the patent fails to specify the reaction conditions. None of these arguments withstand scrutiny. After hearing the same arguments previously, this Court concluded, "[a]t this stage, the record lacks clear and convincing evidence

[10] Defendants' obviousness argument in their motion pertains only to dependent claim 19, which additionally requires that "the nucleic acid sample comprise[] cell-free DNA, and wherein the cell-free DNA comprises tumor DNA." Defendants do not dispute that this limitation is not disclosed or taught in Blomquist but argue that their expert allegedly presented unrebutted "obviousness opinions regarding the use of cell-free DNA." Br. 15. But even if that were true, Defendants' expert's opinions regarding the use of cell-free DNA do nothing to supplement the missing limitation required by all Asserted '708 Claims: "the annealing temperature for the reaction conditions is greater than a melting temperature of the at least 2 primers."

of indefiniteness." D. I. 243 at 12. The record has not changed; no new relevant evidence is proffered. Defendants' motion should be denied; Natera's motion for summary judgment motion of no indefiniteness of the Asserted '708 Claims respectfully should be granted. D.I. 433-2.

The '708 Patent teaches two tools to measure primer melting temperature: (1) empirically using ultraviolet light; or (2) via calculation using Primer3/Santa Lucia software. D.I. 433-2, '708 Patent, 81:53-56, 81:60-66 (discussing the ultraviolet light method), and 61:38-41, 81:43-46 and 236:1-4 (discussing the Primer3 calculator). The Court agreed that such teachings are disclosed. D.I. 243 at 12. No other method is expressly identified in the patent and Defendants point to none. Br. 16. Thus, a skilled artisan would understand the phrase "such as ***the*** empirically measured or calculated Tm" in the specification to indicate generally the two methods identified in the patent. Defendants' contention that this phrase somehow implicates "every technique known to humankind" to measure primer melting temperature is nonsensical. Br. 16. The phrase is "***the*** empirically measured or calculated Tm," ***not "any*** empirically measured or calculated Tm." Defendants made a similar argument during the claim construction proceedings (D.I. 177 at 64), which did not persuade this Court.

The patent discloses that each of the two methods for determining melting temperature are used in "some embodiments." For example, the patent teaches that in some embodiments, the melting temperature is empirically measured and that in other embodiments it is calculated. D.I. 433-2, '708 Patent, 81:53-56 ("In some embodiments, the empirically measured Tm (the actual Tm) is determined by using a thermostatted cell in a UV spectrophotometer."); 61:38-41 ("In some embodiments, the Tm is calculated using the Primer3 program (libprimer3 release 2.2.3) using the built-in SantaLucia parameters (the world wide web at primer3.sourceforge.net)). Defendants' arguments that the patent purportedly should have identified the use of the disclosed methods for

"all embodiments" (when there are two disclosed methods) is illogical. Br. 17. This argument was also unsuccessful during the claim construction proceedings (D.I. 177 at 77).

Defendants' attempts to manufacture lack of definiteness regarding the calculation method are also unavailing. The patent directs a skilled artisan to use Primer3 with the modern SantaLucia values. *See e.g.*, D.I. 433-2, '708 Patent, 61:38-41, 81:42-46 ("In some embodiments, the T_m is calculated using the Primer3 program (libprimer3 release 2.23) ***using the built-in SantaLucia parameters*** (the world wide web at primer3.sourceforge.net, which is hereby incorporated by reference in its entirety).") (emphasis added); D.I. 178, ¶¶ 22-23. Example 25 teaches that the SantaLucia values for Primer3 are "recommended." D.I. 433-2, '708 Patent, 236:1-4. Defendants do not dispute the patent's repeated SantaLucia recommendations but complain that a single reference to "default 0" option somehow causes confusion as to whether to use the SantaLucia or "default" parameters. Br. 17-18.[11] Not so. The reference to default parameters is only in connection for "backward compatib[ility]" to older versions of Primer3. D.I. 178, ¶ 23; D.I. 433-2, '708 Patent, 235:54-57 ("A value of 0 directs primer3 to a backward compatible calculation (in other words, ***the only calculation available in previous version of Primer3***).") (emphasis added). As of the patent's 2014 priority date, there is no confusion that a skilled artisan would use the recommended Primer3 software with the SantaLucia settings. This argument too was unsuccessfully made by Defendants during the claim construction proceedings (D.I. 177, 144).

Defendants repeat the same unsuccessful argument they made previously that other methods may be used to compute melting temperature because Natera had used a different method

[11] Defendants' cite to Natera expert's testimony about the identity of the primers used in Example 25 is a red herring. It is unclear what primer identity has to do with a decision to choose the recommended SantaLucia parameters as opposed to older parameters. To the extent Defendants are insinuating that the patent lacks adequate disclosure, this is clearly untrue given that the patent discloses over 200 ***pages*** of primer sequences. *See e.g.*, D.I. 433-2, '708 Patent, Figs. 34A1-36Q9.

(Bolton & McCarthy) to calculate melting temperature of prior art primers during the prosecution of a different patent. D.I. 177 at 64, 66, 78; Br. 18-20. But Natera also used Primer3/Santa Lucia to calculate melting temperature during that patent prosecution, a fact Defendants admit. (D.I. 177 at 64, 78). Importantly, Natera did not inform the Patent Office that the empirical UV light method would not work. Any insinuation otherwise by Defendants (Br. 19), is simply incorrect. Natera's statements to the Patent Office are entirely consistent with its disclosure in the '708 Patent of the two tools to measure melting temperature. Dr. Spellman's testimony cited by Defendants (Br. 20), does not dispel this fact. As Dr. Spellman testified, it did not matter what method Natera had used during prosecution, both methods gave the same result: primer melting temperature was above the annealing temperature and did not meet the claim limitation.

> Q. Do you have any explanation for why Natera, for the purposes of deciding whether a primer melting temperature satisfies the annealing temperature relationship of the claims, relied upon a method that's not actually disclosed in the patent?
> THE WITNESS:· So in this particular case, the primer has a melting temperature above every possible annealing temperature, no matter how you calculate it. I'm not sure why we care.

Ex. 3, Spellman Tr. 230:14-24 (attorney objection omitted).

Defendants argue that the calculated Primer3/Santa Lucia and the empirical UV light methods yield materially different results. That too was previously raised (D.I. 177 at 78). The Primer3/Santa Lucia software (with the improvement made by Owczarzy and colleagues and available as of the 2014 priority date of the '708 Patent) could determine melting temperature values within 1°C difference from that measured using the UV light method. D.I. 432 at 31-33.

Defendants also previously argued that the '708 Patent fails to specify the conditions for determining the melting temperature (D.I. 177 at 76-77), which the Court rejected. The conditions for determining melting temperature are the same as the ***reaction conditions used***. The specification and the claims make this clear. D.I. 433-2, '708 Patent, Claim 1 ("wherein the

annealing temperature for the ***reaction conditions*** is greater than a melting temperature of the at least 2 primers . . .") (emphasis added). The reaction conditions are important for primer melting temperature calculations, contrary to Defendants' argument. Br. 23. For example, the Primer3 software requires reaction condition inputs, such as concentration of monovalent cations, concentration of divalent cations, DNA concentration and salt correction formula. Ex. 15, Cooper NI Rpt. ¶ 111. Defendants' argument is without merit.

Defendants have failed to show indefiniteness of the Asserted '708 Patent Claims with clear and convincing evidence. Summary judgment of indefiniteness should be denied.

F. DEFENDANTS HAVE FAILED TO CARRY THEIR HEAVY BURDEN TO SHOW THAT THE ASSERTED PATENT CLAIMS ARE NOT ENABLED

Defendants' non-enablement theory rests on an argument contradicted by the patent disclosures and other evidence in the record: that the claimed methods cannot be performed without employing *Natera*'s inventive primer design techniques to minimize primer-dimer formation.[12] "Whether a claim satisfies the enablement requirement is a question of law" but with "factual underpinnings." *Bayer Healthcare LLC v. Baxalta Inc.*, 989 F.3d 964, 980 (Fed. Cir. 2021) (citation and quotations omitted). "Enablement requires that the specification teach those in the art to make and use the invention without undue experimentation." *Id.* (citation omitted). "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." *Martek Biosciences Corp. v. Nutrinova, Inc.*, 579 F.3d 1363, 1378 (Fed. Cir.2009). "Thus, on a motion for summary judgment for invalidity, when a court must construe all inferences in the light most favorable to the patent

[12] While primer design is necessarily required for any PCR reaction—as no PCR reaction can run without primers designed to bind to the template DNA—the asserted claims are not limited to any *specific way* of designing primers. Indeed, Defendants' argument to the contrary during the claim construction proceeding was rejected by the Court. D.I. 243, 5-6; D.I. 177, 11-17, 26.

owner, whose patent is presumed valid, a defendant must meet a high burden indeed." *United Access Techs., LLC v. AT&T Corp., et al*., 11-cv-339 (KAJ), 2021 WL 1840785, at *7 (D. Del. Apr. 30, 2021).

Defendants have failed to carry their heavy burden. Defendants offer not an iota of evidence that a skilled artisan had attempted but failed to perform the claimed methods without employing the specific primer design techniques invented by Natera. Surely, if the claims were truly non-enabled, Defendants' expert could have conducted experiments and adduced evidence of non-enablement. Defendants adduce no such evidence. Indeed, the panoply of accused products offered by Defendants, each of which performs the claimed method, and for which Defendants do not contend to use *Natera's* specific primer-design techniques—demonstrates the opposite: the claimed methods are robust and enabled. Defendants' non-enablement argument is no more than a theoretical exercise untethered to the claims or the disclosure in the Asserted Patents and stitched together by out-of-context select Natera witness testimonies.

1. Defendants' Non-Enablement Theory Is Contradicted by The Patents

Nothing in the Asserted Patents remotely suggest that the claimed methods would not "work" unless the specific primer design technique invented by Natera is employed. Quite the opposite, the patents expressly teach that the claimed methods can be performed without employing *Natera's* primer design techniques. The specifications teach that "highly multiplexed targeted PCR" can be performed "in a highly efficient manner," including by (a) "using a partial or full nesting approach to the targeted PCR"; ***or*** (b) "designing primers that are unlikely to hybridize with one another; or (c) using a combination of both techniques. D.I. 433-1, Ex.1, '814 Patent, 83:36-84:3; D.I. 433-2, '708 Patent, 82:53-83:7. In other words, the claimed methods can be performed without using *Natera's* primer design techniques. The specifications also describe results of experiments conducted using the claimed methods. For example, the specification

teaches that experiments were conducted using the one-sided nested PCR, hemi-nested or triply hemi-nested workflows. D.I. 433-1, Ex. 1, '814 Patent 97:36-38; 98:4-8, 30-33. From these disclosures, a POSA would understand that the claimed methods are a separate invention and can be performed without using the primer design technique disclosed in the patents. Indeed, by improving specificity, the claimed methods reduce primer dimer amplifications ***despite*** the initial primer dimer formation. D.I. 433-1, Ex.4, '220 Patent, 54:58-61; 91:12-16; 98:32-32; 213:3-8.

Against this robust disclosure, Defendants point to a ***single statement*** in the specification that "it is essential to remove the primers" and blow it out of proportion as the essence of Natera's invention. Br. 25.[13] Defendants' assertion ignores the fact that the Asserted Patents disclosed not just a single, but multiple inventions, directed to improving the efficiency and specificity of highly multiplexed targeted PCR, including the nested PCR methods and the use of a higher annealing temperature to reduce non-target amplicons. D.I. 433-1, Ex. 4, '220 Patent, Abstract, 2:54-56, 46:60-66. In sum, Defendants' non-enablement theory conflates inventions and ignores the wealth of factual disputes underlying the *Wands* factors.

Liebel-Flarsheim Co. v. Medrad, Inc., cited by Defendants, is not analogous and in fact supports enablement of the Natera patent claims. 481 F.3d 1371 (Fed. Cir. 2007). In that case, the court had construed the claims as not limited to an injector with a pressure jacket, and therefore the full scope of the claims—injectors with or without a pressure jacket—needed to be enabled. *Id*. at 1378-1379. However, unlike here where the specification ***expressly describes*** using the claimed methods without *Natera's* primer design techniques, the specification in *Liebel-Flarsheim*

[13] Defendants refer to Natera inventor Dr. Bernhard Zimmerman's testimony, but he merely testified about his understanding that the claims themselves do not recite primer-dimers, which is true and undisputed. Br. 26. (citing Ex. E Zimmerman Tr. 233:19-235:3; 226:3-9; 235:24-236:8, 237:18-238:7, 248:3-249:1).

did not describe an injector without a pressure jacket, but in fact ***taught away*** from using such an injector. *Id*. at 1379. Additionally, testimonial evidence in *Liebel-Flarsheim* indicated that an injector without a pressure jacket could not have been produced at the time of filing. *Id.* at 1380. No such evidence has been presented by Defendants here. As discussed further below, Defendants have adduced no real-world evidence that the claimed methods could not be performed without *Natera's* primer design techniques. The claimed methods are enabled.

2. Defendants' Cherry Picking of Natera Witness Testimonies Does Not Satisfy Their Burden on Summary Judgment

Nowhere in the Natera witness excerpts that Defendants identify as support for their non-enablement theory, Br. 26-29, did Natera's witnesses testify that it was not possible to perform the invention of the claims without the use of *Natera's* primer design techniques. With no testimony on point, Defendants concoct purported support for their non-enablement theory based on testimony about primer design ***in general***. This is Defendants' rhetorical sleight of hand: for PCR to work, a primer must bind to the target loci of interest. This is well-known and undisputed. Thus, a primer with sequences complementary to the target must be selected. The Asserted Claims expressly require such selection. For example, the claim terms "target loci," "target specific primers," and "inner target-specific primers" necessarily require selecting target loci and primers that bind to the target loci. Ex. 16, Spellman Rpt. ¶¶ 248-252. A POSA would know that selecting primers necessarily involves designing primer that would bind the target of interest, *i.e.* primer design. Ex. 3, Spellman Tr. 208:11-14 ("So one picks a part of the DNA one wants to amplify. One ***designs primers*** that bind to the regions around that piece of DNA you wish to amplify, and one then instantiates a PCR reaction.") (emphasis added). A POSA would also know that primer design includes selecting a primer that would bind in the right orientation or selecting a primer with an appropriate melting temperature. Ex. 3, Spellman Tr. 195:7-196:3. Where it is apparent

from the primer sequences that the primers would bind to each other, a skilled artisan would know not to use such primers. Ex. 3, Spellman Tr. 196:19-24. These basic primer design techniques were well-known in the art. In fact, Dr. Spellman testified that this was well-known at least when he was in graduate school, if not earlier. Ex. 3, Spellman Tr. 206:17-21.

Defendants, however, ignore this context and make much of Natera witnesses' testimonies when they were merely testifying about "primer design" in general. Br. 26-28. That a particular method of primer design is not required does not mean that the claim must work with no design or deliberately poor design or just any design or it is not enabled. It means that the POSA must be able to practice the invention as claimed, with the POSA's own knowledge and understanding of techniques in the art. For example, Dr. Spellman testified that one cannot perform PCR without using primer design in general, not about primer design technique invented by Natera. Br. 26, 30. Likewise, he merely testified that if no thought is put into designing primers, such that primers are used at random with no rhyme or reason, the PCR would not work or would yield garbage. Br. 27. It is absurd to expect a skilled artisan to ignore his own knowledge and skill in the art and employ primers randomly in a PCR reaction. Dr. Spellman also testified that "examining primers for primer dimer formation is an essential component of PCR at all levels" (Br. 28), but it was in the context of a skilled artisan's common practice of evaluating primer sequences to determine if they could bind to each other. Ex. 3, Spellman Tr. 206:17-21. Natera's expert Dr. Quackenbush similarly testified that in designing primers one would use prior art Primer3 software (Br. 28, 31), which is indisputably used to determine melting temperature of primers, another example of primer design. Likewise, Natera's inventor Dr. Zimmerman testified generally that he would never run experiments without taking measures to avoid primer dimers, ***not*** that he would have to employ *Natera's* primer dimer techniques to perform the claimed methods. Br. 28. Enablement is

evaluated from the perspective of one of ordinary skill in the art armed with his own knowledge of the art, not in vacuum. *Bayer*, 989 F.3d at 982 ("[W]hether a patent is enabled—or requires undue experimentation—are questions that must be viewed from the perspective of one of ordinary skill in the art."). Nothing in the testimonial excerpts suggest that it was impossible to perform the claimed methods without using Natera's primer design techniques.

Defendants also argue—based again on snippets of witness testimony taken out of context and complete disregard of any evidence to the contrary—that the claimed methods would not work for multiplex PCR reactions that go beyond 280,000-plex. As an initial matter, the argument is irrelevant at least with respect to claims 6 and 7 of the '220 patent, which expressly limit the target loci to between 100 and 5000. D.I. 433-1, Ex. 4, '220 Patent, claims 6-7. Defendants appear to accept Dr. Spellman's testimony that a skilled artisan could carry out a 280,000-plex PCR using the claimed methods. Br. 26. Surely then a skilled artisan would be able to carry out a mere 100-plex to 5,000-plex PCR. Moreover, Defendants quibble about Dr. Spellman's testimony pertaining to multiplex PCR beyond 280,000-plex, but this is based on select testimonial excerpts[14] that ignores Dr. Spellman's opinion to the contrary. Dr. Spellman explained that there is necessarily an upper limit on the number of target loci—an individual does not have infinite target loci and one would not amplify every target of an individual; it would defeat the purpose of using the claimed "target specific primers." Ex.16, Spellman Rpt. ¶¶ 262-264.

Dr. Spellman noted the rich and extensive 200-plus page guidance provided by the patents, including: (a) multiple working examples of up to 28,000-plex reactions; (b) detailed sections on the different aspects of the claimed methods, including sections on highly multiplex PCR, ligation

[14] For example, Defendants did not cite Dr. Spellman's testimony that he saw no "fundamental" issue in scaling to 1 million when asked about 1 million-plex. Ex. 3, Spellman Tr. 203:7-16.

adaptors, tagged primers, primers with ligation adaptor binding region, and nesting workflows, targeted PCR, targeted PCR variants; (c) Figures depicting the workflows and experimental results and (d) additional teachings to provide context and further guidance. *See e.g.*, Ex.16, Spellman Rpt. ¶¶ 262-267. Describing the patents as "a lengthy treatise on multiplex PCR" (Ex. 3, Spellman Tr. 154:3-13), Dr. Spellman opined that a POSA would be reasonably confident to amplify up to 280,000 loci, explaining that 280,000-plex is a 10x scale up of 28,000-plex and the patentee had demonstrated 20x scale up from 1,200-plex to 28,000-plex. Ex.16, Spellman Rpt. ¶ 267. "A claim is sufficiently enabled even if 'a considerable amount of experimentation' is necessary, so long as the experimentation 'is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.'" *Vasudevan Software, Inc. v. MicroStrategy, Inc.*, 782 F.3d 671, 684 (Fed. Cir. 2015).[15]

Ultimately, Defendants' out of context selective testimony excerpts not only undermines Defendants' non-enablement theory, but also further underscores the factual disputes between the parties. Natera's expert explained in detail how the *Wands* factors confirm enablement. He opined that the breadth of the asserted claims is narrow, PCR was well-established in the art, multiplex PCR was known although higher-plex reactions were not taught in the art, but a POSA armed with the extensive teachings in the patents including actual working examples would be able to make

[15] Defendants' reliance on *MagSil Corp. v. Hitachi Global Storage Techs., Inc.*, 687 F.3d 1377 (Fed. Cir. 2012) is misplaced. Br. 26, n.4. In *MagSil*, the inventors had not achieved even a 20% change and there were no working examples of 20%, 120%, 604% or 1000% change. *Id*. at 1382. By contrast, the Asserted Patents disclose working examples of 1200-, 2400-, 9600- and 28,000-plex reactions and Dr. Spellman opined that there is necessarily an upper limit on the number of target loci. Ex. 16, Spellman Rpt. ¶¶ 262-267. This is also not a case of art advancing so vastly after the filing of patent application that 600% was achieved many years later, while not even 20% was achieved at the time of filing. 687 F.3d at 1382. Notably, Defendants have adduced no such evidence in this case. "A patentee is not required to provide actual working examples" to sustain an enablement challenge" - rather the burden is on Defendants. *Alcon Research Ltd. v. Barr Laboratories, Inc.,* 745 F.3d 1180, 1189-90 (Fed. Cir. 2014).

and use the full scope of the claims. *See* Spellman Rpt. ¶¶ 223-295. Further, Defendants' non-enablement contentions flat out contradict their arguments as to purported obviousness and alleged routine nature of the claimed methods. Defendants have argued that every step of the claimed methods was allegedly known in the art, Br. 31, and Defendants' expert has opined that the "concept of molecular barcode," "high throughput sequencing," "variables for PCR optimization," optimizing "primer concentration," and "optimiz[ing] experimental conditions" to maximize the percent of amplicons that map to the target locus were also well-known techniques. *See e.g.*, Ex. 16, Spellman Rpt. ¶ 260. At a minimum, this fact intensive *Wands* factors inquiry counsels against summary adjudication of non-enablement, particularly where all inferences must be drawn in Natera's favor.

G. THE PRIORITY APPLICATIONS AND CFDNA PATENTS ADEQUATELY DESCRIBE THE ASSERTED CLAIMS

"Whether the written description requirement is met is a question of fact." *Martek Biosciences Corp. v. Nutrinova, Inc*., 579 F.3d 1363, 1369 (Fed. Cir. 2009). Defendants bear the burden of proving lack of written description by clear and convincing evidence. *Microsoft Corp. v. i4i Ltd. P'ship,* 564 U.S. 91, 100 (2011). Again, Defendants cannot meet this high burden. Defendants argue that the priority applications and the '220, '814, '172 and '482 Patents ("the cfDNA patents") do not describe the claimed inventions as an integrated whole; but that argument lacks merit and is undermined by Defendants' own expert's testimony, the extensive disclosure in the patents, and the detailed opinions of Natera's expert Dr. Spellman. Defendants next argue that the inventors were in possession only of primer-design techniques (which purportedly are necessary "to perform large scale multiplex PCR"). The specification and the priority applications contradict that argument. At a minimum, these disputes raise genuine issues of material fact, particularly in view of Defendants' heightened burden. *Procter & Gamble Co. v. Teva Pharms.*

USA, Inc., 566 F.3d 989, 994 (Fed. Cir. 2009) (citation and quotation omitted).

1. The Priority Applications and the cfDNA Patents Adequately Describe the Claimed Inventions as an Integrated Whole

Defendants proffer evidence cherry picked from witness testimonies taken out of context and complaints about Natera's thorough interrogatory responses. Weighed against this anemic evidentiary showing is Defendants' expert's testimony which contradicts Defendants' position, a 200-page long comprehensive patent disclosure and Natera's expert's detailed opinions.

Defendants' expert Dr. Cooper's testimony undercuts Defendants' argument that the priority applications and the cfDNA Patents do not describe the claimed inventions as an integrated whole. Dr. Cooper testified that Figure 6, disclosed in the priority application No. 13/300,235 ("the '235 priority application", Ex. 10) filed on November 18, 2011, teaches the claimed methods of the cfDNA Patents, as exemplified by claim 1 of the '814 Patent in the table below.

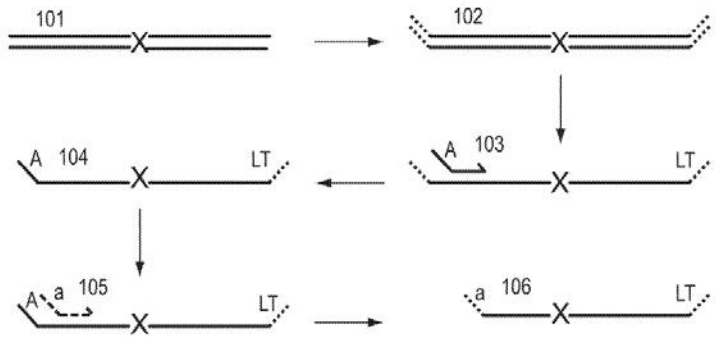

FIG. 6

Claim 1 of the '814 Patent	Defendants' expert Dr. Cooper's testimony
A method for amplifying and sequencing DNA, comprising	Q. So Figure 6 is a representation of a one-sided nested PCR, correct? A. Right. I think so. I think it would take me a while to fully understand all the details here, but yes, I believe that's true.
ligating adaptors to **cell-free DNA** isolated from a biological sample, wherein the adaptors each comprises a universal priming site;	Q. What is 101 in Figure 6? A. That is a representation of an input **DNA** molecule that has -- in this case, I think, they are saying it's a polymorphism at that X that marks something that you would like to sequence or somebody would like to assay.

	Q. What is 102 in Figure 6? A. That is the molecule from 101 with adaptors added at the ends. Q. Are the adaptors depicted by dotted lines at the ends of the DNA molecule? A. Yes, I believe that's correct. Q. How are these adaptors added to the DNA molecule? A. It says "**ligation adaptors**." Q. So the adaptors are ligated to the DNA molecule, is that correct? A. Yes. Q. If you turn to paragraph 316 of the '235 application, which is Exhibit 1241, it provides: "The **method was performed** on libraries of apoptotic supernatants and **pregnancy plasma**." Do you see that? A. I do. Q. Now, this indicates that the applicant had performed this workflow on pregnancy plasma, correct? A. Yeah, yes. Q. And pregnancy plasma includes **cell-free DNA**, correct? A. **Yes**. So what I assume they mean is plasma from a cell-free DNA from the mother and fetus.
performing a first PCR to simultaneously amplify at least 10 target loci using a **universal primer** and at least 10 **target-specific primers** in a single reaction volume;	Q. What is depicted in 103 of Figure 6? A. That is an after amplification from 102, that is a single-stranded representation of one of the amplification products. Q. What is A in 103 of Figure 6? A. That is a primer that is being newly introduced into the next step. Q. Is that a **target-specific primer** that is introduced in this step? A. **I believe it is, yes**. Q. Is the primer introduced -- strike that. Is another primer also introduced at this step? A. Well, they're not showing it, but I believe that it would be -- reverse primer would be on the other end. Q. What is the reverse primer that would be used in 103 step of Figure 6? A. That's something that sticks to the LT portion. Q. So it would be **a primer that is specific to the adaptor**, is that correct? A. **Right**. They are not specifying that, but it certainly would at least partially stick to the LT adaptor, yeah. Q. It could also fully hybridize to the LT adaptor, correct? A. Potentially, sure.
performing a second, **nested PCR** to simultaneously amplify the at least 10 target	Q. What is 104 in Figure 6? A. So that is a product from -- produced after that -- after the primers at the 103 step were used for amplification.

loci using the **universal primer** and at least 10 **inner target-specific primers** in a single reaction volume, wherein at least one of the primers comprises a sequencing tag;	Q. So 104 denotes that PCR product from 103 amplified using target-specific primer A and ligation adaptor-tag-specific primer LT, is that correct? A. Yes, that's right. Q. Is primer LT a **universal primer**? A. I believe in this, yes. I believe so, **yes**. Q. What is shown in 105 of Figure 6? A. Here, they are doing -- there's an extra amplification with a primer that is internal to that104. Q. Is this **a nested PCR step**? A. **Yes**, I believe so. Q. And is **primer small "a" nested with respect to primer capital "A"** from the 103 step? A. I believe that's the representation, **yes**. Q. Is there another primer that is employed in the 105 step of Figure 6? A. Right, I believe they are using LT again. Q. So they are using a **universal primer again**, is that correct? A. That **looks right**. Q. Okay. And what is 106 in Figure 6? A. That appears to be the product from that little "a" to LT. Q. So 106 is the product from 105 **amplified using a nested target-specific [and] universal primer**, is that correct? A. Yeah, that looks correct.
performing high-throughput sequencing to **sequence** the amplified DNA comprising the target loci.	Q. The '235 application further provides in paragraph 0316: "With this workflow around 60 percent of **sequences mapped to the attended targets."** Do you see that? A. I do see that.

Ex. 7, Cooper Tr. (Vol. 2) 254:2-16; 255:4-258:24 (emphasis added).

Additionally, Natera's expert Dr. Spellman laid out in detail that the Natera priority applications and the cfDNA patents adequately describe the claimed inventions. Ex. 16, Spellman Rpt., *see e.g.*, ¶¶ 40-63, 223-299. For example, Dr. Spellman explained: (1) that the priority applications expressly describe the steps as arranged in the claims (*Id*. at ¶¶ 43-49); (2) that the priority applications teach the use of molecular barcodes and sequencing tag in the claimed methods (*Id*. at ¶¶ 49-57); (3) that the priority application teaches working examples using 1200-plex, 2400-plex, 9600-plex reactions (Ex. 10, '235 Application, Examples 7-14); and (4) that a skilled artisan would understand how molecular barcodes and sequencing tag are used in the

claimed methods, which is further supported by Dr. Cooper's opinion that molecular barcodes and high throughput sequencing were well known in the art. (Ex. 11, Cooper Opening Rpt. ¶¶ 126, 164-165); *see Capon v. Eshhar*, 418 F.3d 1349, 1357 (Fed. Cir. 2005) ("The 'written description' requirement must be applied in the context of the particular invention and the state of the knowledge."); *Immunex Corp. v. Sandoz Inc.*, 964 F.3d 1049, 1064 (Fed. Cir. 2020) ("It is well-established that a patent specification need not re-describe known prior art concepts.").

Further, the priority application and the cfDNA Patents disclose, for example, in text and Figure 6 (1) how the method works, (2) the disclosed successful experiments using the depicted method (including with cell-free DNA containing samples) and (3) explaining that primers with sequencing tags can be employed and that individual DNA molecules may be tagged with a molecular barcode. Ex. 10, '235 Application, [201], [261]; D.I. 433-1, Ex. 1, '814 Patent, 86:59-60; 156:29-32. The cfDNA Patents are entitled to priority date of November 18, 2011. *Martek Biosciences Corp. v. Nutrinova, Inc*., 579 F.3d 1363, 1369 (Fed. Cir. 2009) (To be entitled to the filing date of an earlier application, the disclosure in the earlier application must "reasonably convey[] to the artisan that the inventor had possession at that time of the later claimed subject matter," but "the earlier application need not describe the claimed subject matter in precisely the same terms as found in the claims at issue.") (citation omitted).

Contrary to Defendants' contention (Br. 32), this is not a case where disparate elements are scattered across the specification; instead, the entire workflow is described as a whole and the priority application and the issued patents disclose that additional elements such as a sequencing tag or molecular barcode may be included into the workflow. Ex. 16, Spellman Rpt., ¶¶ 40-63, 223-299. Such a disclosure meets the written description requirement. *Ariad Pharms., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010 (It is not necessary that the specification recite

the claimed invention *in haec verba*") (en banc); *Indivior Inc. v. Dr. Reddy's Labs., S.A.*, 930 F.3d 1325, 1346 (Fed. Cir. 2019) (rejecting DRL's argument that failure of priority application to disclose any embodiment with the precise combination of components as claimed renders the claim inadequately described, when there is other adequate disclosure in the application).

Defendants focus only on evidence they think is helpful and misinterpretation of cherry-picked excerpts of Natera's expert's testimony. For example, Defendants contend Dr. Spellman confirmed that there was no disclosure of the claimed invention as a whole in the '508 Application, Br. at 33-34. But Dr. Spellman testified that he "has an extensive discussion of the '508" application in his expert report and that he opined that the '508 application discloses the claimed invention. Ex. 3, Spellman Tr. 263:7-264:1. As to the '235 Application, Dr. Spellman offered to read the patent application "carefully and lining it all up," explaining that "this is an extensive specification" and "within this document are all the claims." Ex. 3, Spellman Tr. 185:2-21. Defendants demurred. Defendants should not now be allowed to portray Dr. Spellman's testimony as limited to the select excerpts they identify. Likewise, with respect to barcodes, Dr. Spellman testified that "[t]hey're extensively documented in this . . . specification," (Ex. 3, Spellman Tr. 186: 21-23); yet Defendants focus on Dr. Spellman's testimony on a single sentence in the patent, taking it out of context. Ex. 3, Spellman Tr. 189:4-21.

Remarkably, after trumpeting Dr. Spellman's purported inability to identify support for the entire claimed invention, Defendants take the opposite tack with Natera's interrogatory responses and complain that Natera provided too much information. Br. 35. But Natera's interrogatory response is extensive for the simple reason that the patent specification is a rich trove of detailed information about the inventions—"a lengthy treatise on multiplex PCR" (Ex. 3, Spellman Tr. 154:3-13). It strains credulity that Defendants could not comprehend the precise workflow

depicted in the patent figures and explained in detail in the patent specification, particularly when their own expert had no difficulty explaining how one of the figures in the patent matched to the claimed methods, as discussed above. Defendants certainly cannot claim their own inability to understand the document merits summary judgment in their favor.

2. Inventors Were in Possession of The Claimed Methods as Of The Priority Date

Defendants fail to show why the inventors did not possess the claimed methods or support their allegation that the inventors were "in possession solely of techniques that relied upon primer design." Br. 29.

Defendants' argument for lack of possession is essentially a restatement of their non-enablement argument that the only way of doing large scale multiplex PCR is by employing *Natera's* primer design techniques. Br. 30-31. But this argument fails for the reasons described previously. *See supra* Section II.F. Defendants' reference to passages in the patent disclosing *Natera's* primer design technique (Br. 30) merely shows that Natera had described them as one of the ways to improve the efficiency of highly multiplexed targeted PCR.[16]

None of the cases cited by Defendants (Br. 31, 36) compel a different conclusion. In each of these cases, the specification did not teach an embodiment covered by the claims, unlike here where the specification teaches the claimed methods without using *Natera's* primer design techniques. *See e.g.*, *LizardTech, Inc. v. Earth Res. Mapping, Inc.*, 424 F.3d 1336, 1344 (Fed. Cir. 2005) ("the specification provides only one method for creating a seamless DWT, which is to maintain updated sums of DWT coefficients."); *ICU Med., Inc. v. Alaris Med. Sys., Inc.*, 558 F.3d

[16] Here again, Defendants obfuscate facts. For example, Defendants state, "This alleged 'surprising discovery' is so critical to the alleged inventions that Natera's own expert even relies upon it as an indicator of non-obviousness." Br. 30. But the non-obviousness opinion concerned the '708 Patent, and Defendants are not asserting that the '708 Patent is not entitled to its priority date or otherwise inadequately described.

1368, 1378 (Fed. Cir. 2009) ("the specification describes only medical valves with spikes"); *Rivera v. Int'l Trade Commission*, 857 F.3d 1315, 1322 (Fed. Cir. 2017) ("The specification here does not teach a container with an integrated filter"); *Driessen v. Sony Music Ent.*, 640 F. App'x 892, 896 (Fed. Cir. 2016) ("The terms 'selling computer,' 'payment message,' and 'authorization message' are not present anywhere in the specification or original provisional application.").

Defendants' argument that the "inventors were in possession solely of techniques that relied upon primer design" (Br. 29-31), and not the claimed methods, flies in the face of the extensive disclosure of the claimed methods, as discussed above. Much as Defendants desperately wish for, this is not a case of a party claiming broader than its invention (Br. 36), but of a party wishing to profit from another's invention. Defendants cannot wish away Natera's extensive disclosure of its inventions. Summary judgment is improper.

H. DEFENDANTS HAVE FAILED TO SHOW THAT THE IDENTIFIED EXPERT OPINIONS SHOULD BE EXCLUDED

"[E]xpert testimony is admissible if it 'is based on sufficient facts or data,' 'the testimony is the product of reliable principles and methods,' and 'the expert has reliably applied the principles and methods to the facts of the case.'" *bioMerieux, S.A. v. Hologic, Inc.*, No. 18-21-LPS, 2020 WL 327161, at *1 (D. Del. Jan. 21, 2020) (citing Fed. R. Evid. 702(b)-(d)) "Rule 702 embodies a liberal policy of admissibility." *Pineda v. Ford Motor Co.,* 520 F.3d 237, 243 (3d Cir. 2008). "Where the methodology is sound and the evidence relied upon is sufficiently related to the case, disputes over the expert's credibility or over the accuracy of the underlying facts are for the jury." *Summit 6, LLC v. Samsung Elecs. Co.*, 802 F.3d 1283, 1299 (Fed. Cir. 2015).

1. Dr. Spellman's Opinions on Faham Are Supported, Admissible And Should Not Be Excluded

Defendants seek to exclude Dr. Spellman's rebuttal opinions regarding a purported prior art reference, Faham, on the sole basis that it is "conclusory and irrelevant." Br. 36-37. But rather

than providing "just two pages" of opinion on the issue as Defendants incorrectly assert,[17] Dr. Spellman provided a detailed discussion of what the Faham reference discloses and why it does not anticipate or render obvious the asserted claims. Dr. Spellman's opinions are based on his careful analysis of Faham and his more than 25 years of experience in the field of genomic technologies using panel-based sequencing approaches. Simply put, Dr. Spellman's opinions are relevant, reliable and would be helpful to the trier of fact.

Specifically, Dr. Spellman explained that Faham is directed to methods of using "***clonotype profiles***" to detect and monitor disease or non-disease conditions – an entirely different method than that disclosed in the asserted claims. Ex. 16, Spellman Rpt. ¶¶ 131-132; Ex. 3, Spellman Tr. 167:19-172:1 (Faham discloses "a completely different way of solving this problem."). He identified several limitations missing in Faham and provided a factual analysis showing that the method described in Faham does not use universal primers and all of the primers used are target-specific primers because they bind to a specific region in the T cell receptor ("TCR") or B cell receptor ("BCR"). Ex. 16, Spellman Rpt. ¶¶ 133-134. Dr. Spellman also explained his disagreement with Defendants' expert's contrary opinion that such targeta universal primer. *Id.* at ¶ 135; *see also* Ex. 3, Spellman Tr. 161:20-165:8 (explaining his disagreement with Dr. Cooper's opinion because Faham states "very clearly" that "[t]his primer is not binding to a universal priming sequence in the adaptor, but is specific to a target sequence.").

Following the discussion of Faham vis-à-vis the patented methods, Dr. Spellman set forth his analysis regarding the effect of this prior art reference on the validity of the asserted claims by showing, on a claim-by-claim, limitation-by-limitation basis, that Faham does not teach certain claim limitations, including "performing a first PCR reaction using a universal primer" or

[17] This is the second time Defendants have distorted Dr. Spellman's expert opinion.

"performing a second, nested PCR using at least 10 inner target-specific primers in a single reaction volume." Ex. 16, Spellman Rpt. ¶ 159; *see also id.* at ¶ 134. Dr. Spellman also explained why a POSA would not be motivated or have a reasonable expectation of success by combining Faham with another prior art reference (Broude), as Defendants' expert asserts, to practice the claimed methods. *Id.* at ¶ 160; *see also id.* at ¶¶ 131-132; Ex. 3, Spellman Tr. 167:19-172:1.

In short, the record shows that Defendants' ground for challenging the reliability of Dr. Spellman's opinions is meritless. Indeed, Defendants' criticisms go not to reliability, but rather to the weight and credibility of Dr. Spellman's opinions, which is not a proper basis to exclude an expert opinion. As this Court has explained, "[t]he weight and credibility of an expert's testimony may be challenged through [v]igorous cross-examination, presentation of contrary evidence, and careful instruction on the burden of proof." *Massimo Corp. v. Philips Elec. N. Am. Corp.*, 62 F. Supp. 3d 368, 388 (D. Del. 2014); *see also Inline Connection Corp. v. AOL Time Warner Inc.*, 470 F. Supp. 2d 435, 439 (D. Del. 2007) ("the burden of exploring the facts and assumptions underlying the testimony of an expert witness [is] on opposing counsel during cross-examination" (citation omitted)). A *Daubert* motion is not an appropriate vehicle for such challenges.

The cases Defendants rely on are factually dissimilar and thus inapposite. Br. 37. In *Magnetar Techs. Corp. v Six Flags Theme Parks Inc.*, No. 07-127-LPS, 2014 WL 529983, at *6 (D. Del. Feb. 7, 2014), the plaintiff's expert failed to compare ***any*** claim element to the accused product to support his literal infringement or DOE conclusions. The remaining non-binding cases fare no better. In the two *Genband* cases, the technical expert provided ***only*** conclusory statements concerning DOE and diligence in reduction to practice. *Genband US LLC v. Metaswitch Networks Corp.*, No. 2014-cv-33-JRG, 2016 WL 3475688, at *2 (E.D. Tex. Jan. 7, 2016); *Genband US LLC v. Metaswitch Networks Corp.*, No. 2014-cv-33-JRG, 2016 WL 98745, at *4 (E.D. Tex. Jan. 8,

2016). Notably, the court did not strike testimony on other issues where the expert's rebuttal opinions were supported by the expert's reasoning and specialized knowledge as an expert. Likewise, in *Sprint Commc'ns Co. L.P. v. Vonage Holdings Corp.*, No. 05-2433-JWL, 2007 WL 2572417, at *2 (D. Kan. Sept. 4, 2007), it was undisputed that the expert performed ***no*** obviousness analysis and only provided "concluding summaries" that were no more than "boilerplate" language "intended to serve as placeholders" only. In *Elder v. Tanner*, 205 F.R.D. 190, 194 (E.D. Tex. 2001), the experts provided ultimate opinions regarding infringement, anticipation, and obviousness "without any elaboration or reasoning."

Unlike the experts whose testimonies were excluded, here, as discussed above, Dr. Spellman has provided the supporting analysis for his opinions regarding Faham. *See, e.g.*, *EMC Corp. v. Pure Storage, Inc.*, 154 F. Supp. 3d 81, 94 (D. Del. Feb. 11, 2016) (denying motion to exclude expert's opinions where the expert "based his opinion, not on speculation, but on analysis of Pure's source code and his experience in the field."); *RSA Protective Techs., LLC v. Delta Scientific Corp.*, No. LA CV19-06024 JAK (PLxAx), 2021 WL 4978462, at *8 (C.D. Cal. Oct. 20, 2021) (denying motion to exclude expert opinions regarding written description "because the evidence on which he relied in forming his opinions is sufficiently tied to the facts of the case"); *Tinnus Enters., LLC v. Telebrands Corp.*, No. 6:16-CV-00033-RWS, 2017 WL 3457104, at *4 (E.D. Tex. Aug. 11, 2017) (denying motion to strike expert opinions where Defendants' critiques were only that the opinions were "overly simple, containing a 'high level regurgitation' of information and lacking in explanation for his conclusions" which "go to the weight of his opinions and not the admissibility."). There is nothing flawed or improper about Dr. Spellman's opinions, or the methodology by which he arrived at them. Any dispute that Defendants have with his opinions are properly the subject of cross examination at trial – not *Daubert*.

2. Drs. Spellman and Quackenbush's Opinions that Natera's Signatera Assay Practices the '708 Patent Are Proper[18]

In challenging Drs. Spellman and Quackenbush's opinions that Natera's Signatera assay practices the '708 Patent, Defendants insist that Natera's experts must, but failed to, provide a limitation-by-limitation analysis. Br. 37-39. Not so. Natera's expert Dr. Spellman provided the requisite analysis. Moreover, Defendants' position about the need for a limitation-by-limitation analysis has been rejected and Defendants fail to cite any case law to the contrary. *See Morpho Detection, Inc. v. Smiths Detection, Inc*., 957 F. Supp. 2d 655, 673-74 n.22 (E.D. Va. 2013).

The *Morpho* case is illustrative. In *Morpho,* the defendant argued that Morpho's expert was required to provide "the equivalent of a claim by claim infringement analysis" on Morpho's product prior to proffering an opinion that the product was a commercial embodiment of the asserted patent. *Id.* The court rejected that argument, noting (as here) that the defendant "cites no law in support of this contention" and "fails to demonstrate a sound legal basis for its argument [.]" *Id.* The court further noted that even if the evidence was somehow lacking regarding whether the product was practicing a specific claimed feature, the product remained relevant to the jury's analysis of the secondary considerations of nonobviousness. *Id.*

Defendants' argument is further undermined by Dr. Spellman's Report expressly citing to and incorporating Natera's interrogatory response, which provided a *detailed claim chart* showing, on an element-by-element basis how Signatera practices the '708 Patent claims. *See* Ex. 16, Spellman Rpt. ¶ 212; Ex. 9, 9/3/2021 Natera's Second Supplemental Responses to ArcherDX's Third Set of Interrogatories (No. 10). Dr. Spellman also provided five paragraphs of detail and additional citations to documents showing that Signatera practices the Asserted Claims of the '708 Patent. *See* Ex. 16, Spellman Rpt. ¶¶ 194-199, 212. Any questions about whether Signatera practices the '708 Patent are for the jury.

Defendants argue that Dr. Spellman fails to reliably assess whether Signatera practices the claim element "the annealing temperature for the reaction condition is greater than a melting

[18] Natera's experts will not offer testimony on whether Signatera practices other Natera patents. As such, Defendants' *Daubert* motion relating to patents other than the '708 patent is moot.

temperature of the at least 2 primers" because Dr. Spellman allegedly: (1) relied on a Natera document without conducting his own experiments; (2) failed to apply the Court's claim construction; and (3) did not know how the Signatera primer melting temperatures are calculated. Br. 37-38. Defendants' arguments are unsupportable by law.

First, as discussed above, Dr. Spellman is not required to conduct his own separate limitation-by-limitation analysis. Nor is he required to conduct his own experiments as he is permitted to rely upon any form of probative evidence. Fed. R. Evid. 702. Second, Dr. Spellman properly applied this Court's claim construction. *See* Section II.B., *supra*. Third, Dr. Spellman never testified that "he had no idea how the Signatera primer melting temperatures are calculated" as Defendants allege (Br. 38); he simply stated that he "did not recall if Signatera discloses its method for calculating or measuring its melting temperatures." D.I. 434, Ex. B, 40:7-9. At best, Defendants' arguments go to the weight, not admissibility, of Dr. Spellman's opinions. *See Summit 6, LLC v. Samsung Elecs. Co.*, 802 F.3d 1283, 1299 (Fed. Cir. 2015) ("Where the methodology is sound and the evidence relied upon is sufficiently related to the case, disputes over the expert's credibility or over the accuracy of the underlying facts are for the jury.").

Defendants likewise argue that Dr. Quackenbush did no analysis or claim mapping to determine which claims of the '708 Patent Signatera practices. Br. 38-39. As discussed above, claim mapping is not required to establish a commercial embodiment. Dr. Quackenbush testified that he is familiar with Signatera, and he had reviewed, in detail, the '708 Patent. Ex. 6, Quackenbush Tr. 13:13-14; Ex. 13, Quackenbush Rpt. ¶¶ 331-423. Again, these are weight, not admissibility issues.

3. Dr. Spellman And Mr. Stoll's Opinions Are Admissible to Rebut Defendants' Improper Inventorship Claim And Dr. Cooper's Opinions On The Subject

Defendants seek to exclude the entirety of Dr. Spellman and Mr. Stoll's *rebuttal* testimony on the topic of inventorship. Dr. Spellman and Mr. Stoll's opinions relating to inventorship are a direct response to Defendants' expert Dr. Cooper's legally deficient and factually unsupported

opinions on the subject, which Natera is seeking to exclude. D.I. 432 at 40-41. If the Court grants Natera's summary judgment motion of no invalidity based on improper inventorship and precludes Dr. Cooper to testify on inventorship issues, Natera's experts need not offer any rebuttal expert testimony on the subject, and Defendants' motion to exclude should be denied as moot.

Should Defendants be permitted to raise alleged improper inventorship claims and Dr. Cooper be allowed to testify on inventorship issues however, Natera's experts should be allowed to rebut. Defendants' chief complaint with both Dr. Spellman and Dr. Stoll is that "[n]either expert performed any analysis of information regarding what the inventors actually worked on and whether this might have reflected a material contribution to the alleged inventions." Br. 39. That is a red herring. Neither Dr. Spellman nor Mr. Stoll needed to *establish* that inventorship of the Asserted Patents is correct – it is already presumed to be correct by law.[19] It is Defendants who bear the burden of showing clearly and convincingly that the patents are invalid due to improper inventorship – not Natera.[20] What Dr. Spellman and Mr. Stoll did offer were opinions – based on their respective expertise – about why Defendants' and Dr. Cooper's inventorship analysis is flawed. Defendants have identified no reason why such opinions should be excluded. Indeed, to the extent Dr. Cooper were allowed to testify on inventorship issues, Dr. Spellman and Mr. Stoll's rebuttal testimony would be helpful to the trier of fact and should be admitted.

[19] Defendants' motion would more properly be directed at their own expert, who failed to offer any opinions on "the laboratory notebooks," and indeed their own inventorship case, as Defendants never identified any lab notebooks in response to any contention. Dr. Cooper merely re-states cherry-picked excerpts of Natera witness testimony untethered to each of the asserted claims and purports to tell the trier of fact what the witnesses meant. And as set forth in Natera's *Daubert* motion to exclude Defendants' expert, Dr. Gregory Cooper's opinions on inventorship, Dr. Cooper failed to undertake a proper claim-by-claim analysis of inventorship or evaluation of the contribution of the inventors to each claim. D.I. 432 at 40-41.

[20] *See* Natera's motion for summary judgment of no invalidity based on improper inventorship. D.I. 432 at 22-26.

Dr. Spellman provided rebuttal opinions to Dr. Cooper's inventorship analysis based on his expertise in the field of genomic technologies for the analysis of cell-free DNA.[21] Ex. 16, Spellman Rpt. ¶¶ 1-8; *see also* Ex. 21, Spellman CV. For example, Dr. Cooper's opinion rests on the faulty premise that, rather than analyze the claims, he can ascertain inventorship based on his interpretation of whether select deposition testimony suggests that a given individual worked on "techniques for avoiding primer dimers in multiplex PCR." Ex. 11, Cooper Opening Rpt. ¶¶ 937-939. Dr. Spellman provided detailed rebuttal opinions on this mischaracterization of the Asserted cfDNA Patents' disclosures and claimed inventions. Ex. 16, Spellman Rebuttal Rpt. ¶¶ 223-246. Defendants do not address any of these opinions in their *Daubert* motion.

Likewise, Mr. Stoll provided rebuttal opinions to Dr. Cooper's inventorship analysis based on his nearly 30 years of experience at the USPTO, and his opinions are limited to the practices and procedures of the USPTO.[22] Ex. 17, Stoll Rebuttal Rpt. ¶¶ 5-18; *see also* Ex. 20, Stoll CV. For example, Mr. Stoll rebutted Dr. Cooper's vague and conclusory opinion that the Asserted cfDNA Patents "do not comply with the inventorship requirements." Ex. 11, Cooper Rpt. ¶ 934. Mr. Stoll pointed out that Dr. Cooper failed to articulate what "inventorship requirements" he was referring to. Ex. 17, Stoll Rebuttal Rpt. ¶ 148. In light of such failure, Mr. Stoll provided opinions regarding the USPTO practices and procedures governing inventorship, including the practices and procedures governing correction of inventorship. *Id.* at ¶¶ 42-45; 147; 149-156. Specifically, Mr. Stoll explained that each of the individuals who have been added as inventors are claiming themselves to be inventors, while none of the individuals who have been removed as inventors object to being removed. *Id.* at ¶ 151. Further, Mr. Stoll opined that the request to correct

[21] Defendants do not challenge Dr. Spellman's qualifications as a technical expert.
[22] Defendants do not challenge Mr. Stoll's qualifications as an expert in USPTO practices and procedures.

inventorship and signed statements by the named inventors complied with all of the relevant regulations and guidelines of the USPTO and were properly accepted as such, as evidenced by the Director's issuance of the certificates of correction to inventorship. *Id.* at ¶¶ 152-156.

Defendants also do not address any of these opinions in their *Daubert* motion. Nor could they, as this Court has permitted testimony from such experts "so long as the testimony is clearly related to the ins and outs of internal PTO practices and procedures." *W.L. Gore & Assoc., Inc. v. C.R. Bard, Inc.*, No. 11-515-LPS, 2015 WL 12815314, at *3 (D. Del. Nov. 20, 2015); *see also Brigham & Women's Hosp. Inc. v. Teva Pharm. USA, Inc.*, No. 08-464, 2010 WL 3907490, at *1-2 (D. Del. Sept. 21, 2010) (explaining that "[t]he law permits experts in patent cases to offer [ ] testimony" regarding "the practices and procedures of the PTO").

Defendants' motion does little more than admit that they lack evidence to carry their burden and their own expert did not review the evidence he would have needed to review to offer an opinion that Defendants had met their burden. Defendants should not be permitted to use a *Daubert* motion to preclude rebuttal to their deficient inventorship theory.

4. Mr. Wojcik Provided Sound Opinions Anchored in the Governing Safe Harbor Case Law

Defendants' motion founders on their incorrect characterization of Mr. Wojcik's opinions and their sweeping Safe Harbor arguments that the Court did not accept when denying Defendants' Rule 12(c) Motion. *See* D.I. 59, Hrg. Tr. at 22:7-24:13 (denying Rule12c Motion on Safe Harbor.) This Court's Rule 12(c) denial was "guided" by the Federal Circuit's 2019 *Amgen v. Hospira* decision. 944 F.3d 1327, 1339 (Fed. Cir. 2019). That decision, and others, hold that Section 271(e)(1) liability does not attach to infringement if the infringing act was performed "solely for uses reasonably related to the development and submission of information" to the FDA. 35 U.S.C. § 271(e)(1); *Amgen*, 944 F.3d at 1338. "Whether a 'use' falls within the Safe Harbor Exemption

is a fact-based issue." *Chang v. Biosucess Biotech Co*., 76 F. Supp. 3d 1022, 1036 (C.D. Cal. 2014). *Amgen* reaffirmed that the Safe Harbor does not apply to all pre-approval activity:

> To the extent Hospira suggests the Safe Harbor exemption always applies in the pre-approval context . . ., we have previously rejected that reading of the statute. It is incorrect to "assume[] that all otherwise infringing activities are exempt if conducted during the period before the regulatory approval is granted."

Amgen, 944 F.3d at 1339, n.2 (quoting *Amgen Inc. v. Int'l Trade Comm'n*, 565 F.3d 846, 852 (Fed. Cir. 2009)).

Relevant here, the *Amgen* decision reflects the type of expert testimony that is admissible. There, Amgen's expert testified on whether the batches at issue were or "were not manufactured 'solely for uses reasonably related to the development and submission of information' to the FDA." *Id.* at 1340. Admissible testimony included whether certain stability testing was or was not required by the FDA, and whether the continued process verification was part of a commercial process and not reasonably related to submission of data to the FDA. *Id.* Based on this and other probative expert testimony on the facts and FDA procedures and requirements, as well as Defendants' own admissions, Judge Andrews denied Defendants' JMOL request and the Federal Circuit affirmed. *Id*. S*ee also Amgen Inc. v. Hospira, Inc*., 336 F. Supp. 3d 333, 343-44 (D. Del. 2018) (FDA guidance requires only three batches to demonstrate stability for FDA approval).

So too here is the testimony of Mr. Wojcik probative and admissible. Mr. Wojcik was apprised of and understood the correct legal standard as stated in his report, including that the Safe Harbor extends only to each accused activity "for uses reasonably related to the development and submission of information" to the FDA. *See* Ex. 12, Wojcik Rpt. ¶ 18-19; *see Amgen*, 944 F.3d at 1339. Mr. Wojcik was correctly informed and understood "that each of the accused uses must be evaluated separately to determine whether the Safe Harbor applies." *Id*. Mr. Wojcik properly examined each act of infringement and opined on whether the uses were "for uses reasonably

related to submitting information to the FDA." *See, e.g.*, Ex. 12, Wojcik Rpt. ¶¶ 70-114; *see Amgen*, 944 F.3d at 1339. This included whether certain activities were required for an FDA submission from a regulatory perspective. *See, e.g.*, Ex. 12, Wojcik Rpt. ¶¶ 83-91 ("Such retrospective studies are not type of uses that are reasonably related to FDA approval. ("PMA Clinical Studies, Valid Scientific Evidence (https://www.fda.gov/medicaldevices/premarket-approval-pma/pma-clinical-studies").

Defendants contend that Mr. Wojcik testified that "he is not actually an expert in the Safe Harbor" and that he relied on instructions from the attorneys. Br. 41. But Mr. Wojcik did exactly what a non-legal expert is supposed to do—rely on counsel for guidance on the law and apply the law to the facts based on his or her area of expertise. There is no dispute as to his great expertise on the FDA regulatory process and that the instructions from counsel on the law are firmly grounded in the proper Safe Harbor inquiry. *See Shire Viropharma Inc. v. CSL Behring LLC*, No. CV 17-414, 2021 WL 1227097, at *2 (D. Del. Mar. 31, 2021) (*Daubert* requires qualification, reliability and fit); *Amgen*, 944 F.3d at 1339.

Defendants complain that Mr. Wojcik needs to be an expert on the governing Safe Harbor law. Br. 41. That is legally incorrect. "The District court 'must ensure that an expert does not testify as to the governing law of the case.'" *Shire Viropharma Inc.,* at *14 (citing *Berckeley Inv. Grp., Ltd. v. Colkitt*, 455 F.3d 195, 217 (3d Cir. 2006). Expert witnesses are prohibited from rendering a legal opinion because "it would usurp the District Court's pivotal role in explaining the law to the jury." *Id.* Mr. Wojcik's opinions are helpful to the jury and are grounded in the proper Safe Harbor inquiry and jury instructions under *Amgen*, 944 F.3d at 1339.

a. Mr. Wojcik's Opinions are Not Contrary to the Law

Defendants invite the Court to ignore the testimony and opinions set forth in Mr. Wojcik's deposition transcript and expert report, and to instead assess Mr. Wojcik's testimony and opinions

in an alternate reality of Defendants' own making. To support their incorrect narrative about Mr. Wojcik's opinions, Defendants' strip his testimony from its context and pop it up as if it supports Defendants' arguments. Defendants' arguments do not withstand scrutiny.

Defendants contend that Mr. Wojcik simply testified that the Safe Harbor is limited to development of information for an FDA submission and that preclinical studies that fail to result in a final FDA submission are not covered. Br. 42 (points one and two). But in fact, Mr. Wojcik testified: "Q. And your position is that the safe harbor does not apply to uses that happen during research and development, right? WITNESS: Not exactly." Ex. 5, Wojcik Tr. 87:22-88:2. Regarding preclinical studies, Mr. Wojcik testified: "I am not aware of any rule that preclinical studies are excluded from safe harbor." *Id*. at 92:20-21. Defendants take Mr. Wojcik's testimony out of context, claiming that he testified that there must be an intent to file a final regulatory submission, when in fact Mr. Wojcik was only testifying on the specifics of *an IDE* and only agreeing "*in general*" to Defendants' hypothetical. Ex. 5, Wojcik Tr. 75:3-14. Mr. Wojcik plainly explained that a regulatory submission need ***not*** occur. *See id*. at 74:14-19 (Q. "For the safe harbor to apply, does it need to ultimately end in that submission? WITNESS: "*In general no*. I think, if the intent was there and the decision after the fact was made to no longer pursue, that's still covered.") (emphasis added).

Defendants next wrongly characterize Mr. Wojcik's testimony as always requiring that the protected activity be conducted in conformity with the FDA's good laboratory practices and design controls. Br. 42 (point 3). Defendants are wrong again. He testified that a "blanket statement of it does or is not covered or is covered is difficult to answer without more context." Ex. 5, Wojcik Tr. 69:6-13. He further testified that it's not entirely correct that for Safe Harbor to apply that data needs to be taken according to cGMP or cGLP requirements. Ex. 5, Wojick Tr. at 68:4-16.

Likewise, he imposed no blanket requirement that the Safe Harbor had to adhere to CFR 820.30 design controls and identified circumstances outside of the CFR. *Id.* at 94:3-25.

Defendants claim that Mr. Wojcik opined that the Safe Harbor "***only***" applies for 510k, 510k, PMA, or de novo FDA submissions (Br. 42-43 (point 4)). But Mr. Wojcik actually testified: "If safe harbor does, in fact, apply, then that does infer that there is a submission intended. Q. By submission, you mean 510(k), PMS, or de novo? A. Correct." Ex. 5, Wojcik Tr. 76:24-77:8. Next Defendants claim that Mr. Wojcik opined that "the Safe Harbor does not apply to uses supporting a 'Q submission.'" Br. 43. But that again is not what Mr. Wojcik said and none of Defendants' cites support their characterization. *See id.* at 87:4-11; 209:4-8; Ex. 12, Wojcik Rpt. ¶ 58.

Defendants wrongly characterize Mr. Wojcik's testimony as stating that the Safe Harbor does "not apply to uses that occur in the research and development stage." Br. 43 (point 5). But as addressed above, he quite plainly testified "not exactly" to that very question. Ex. 5, Wojcik Tr. 87:22-88:2. He also testified, that "I'm not aware of any rule that preclinical studies are excluded from safe harbor." *Id*. at 92:20-21.

Defendants attack Mr. Wojcik's expert report as erroneously excluding five categories of activities. Br. 44. Defendants are both factually and legally incorrect:

- There is no dispute that the Safe Harbor applies to more than just certain FDA submissions and Mr. Wojcik did not opine (or testify) to the contrary. *See, e.g.*, Ex. 12, Wojcik Rpt. ¶¶ 38-45. But the fact that certain types of submissions *are not being pursued is probative evidence* of whether an accused infringing act is *reasonably related to* submission of information to the FDA.
- Defendants point to preclinical studies. But there is no blanket rule one way or the other whether a specific preclinical study, is or is not within the Safe Harbor's confines. And nowhere in Mr. Wojcik's report did he categorically exclude all preclinical studies. *Merck* creates no such blanket rule. Indeed, the exemption "*does not globally embrace all experimental activity that at some point, however attenuated, may lead to an FDA approval process*." *Merck v. Integra,* 54 U.S. 193, 204-05 (2005) (emphasis added) (quoting *Merck v. Integra*, 331 F.3d 860, 867 (Fed. Cir. 2003) and noting "we do not quibble with the latter statement").

- Defendants contend that Mr. Wojcik excluded all retrospective relying on *Merck* and reproducibility studies reasonably related to an FDA submission. First, Defendants reliance on *Merck* is misplaced. *Merck* imposes no such blanket rule, *supra,* and Defendants fail to address the factual context that Mr. Wojcik's report addresses—namely the manner in which Defendants perform PCM testing. *See, e.g.*, Ex.12, Wojcik Rpt. ¶¶ 68, 73-79, 84, and 114.

- Defendants next complain that Mr. Wojcik categorically excluded all R&D uses undertaken before the creation of a design history file. First, Mr. Wojcik's report includes no such exclusion. Mr. Wojcik opined on the application of the Safe Harbor based on Defendants' testimony on PCM product development, trial stages, research use only trials, PCM intended uses, chain of custody of samples, study protocols, regulatory submissions, and whether any design history file assembly had begun. *See* Ex.12, Wojcik Rpt. at ¶¶ 68-79. Second, there is no such rule in *Merck*, and each case depends upon its factual context. *See Amgen*, 944 F.3d at 1339.

Defendants' incorrect charactization of Paragraph 53 of Mr. Wojcik's report is especially egregious. This particular paragraph is about a general overview of the life cycle of an *in vitro* diagnostic; Mr. Wojcik did not even opine on safe harbor uses in this paragraph. This exemplifies Defendants' distortion of Mr. Wojcik's opinions.

b. Mr. Wojcik's Opinions are Reliable

Defendants continue to distort Mr. Wojcik's testimony, asserting that "they are based on a misunderstanding and/or mischaracterization of ***the factual evidence***." Br. 44-45 (emphasis added). Defendants' mischaracterizations aside, their disagreement with Mr. Wojcik's interpretation of the factual evidence is not grounds for excluding his testimony. Defendants are free to cross-exam Mr. Wojcik at trial on any fact they contend Mr. Wojcik got wrong. *Daubert v. Merrell Dow Pharms*., 509 U.S. 579, 596 (U.S. 1993); *Summit 6, LLC v. Samsung Elecs. Co*., 802 F.3d 1283, 1299 (Fed. Cir. 2015).

These incorrect characterizations do not withstand scrutiny. Mr. Wojcik's Report states that, "Defendants 'have not submitted any IVD filings on PCM.'" Ex. 12, Wojcik Rpt. ¶ 76 (citing

Holwick Tr. 79:14-15)," Defendants misinterpret this statement to say that "Mr. Wojcik also argued that Defendants had no intention to submit a PCM IVD filing," but that is not what his Report states. Br. 45. As for the other purported "misunderstandings," Mr. Wojcik was questioned about them and gave his testimony. Br. 43-45.

Likewise, and contrary to Defendants' assertions, on paragraphs 73 to 75 of his report, Mr. Wojcik testified that Defendants' uses of PCM for RUO projects with BMS, the General Hospital and Memorial Sloan Kettering *are not* for the purpose of FDA approval as evidenced by the fact that they are identified as *research use only*. Ex. 5, Wojcik Tr. 184:15-185:1. That is probative evidence that the uses are not tied to a FDA submission. Defendants incorrectly represent that Mr. Wojcik "agreed that the FDA submission referenced in his citation was related to a PCM FDA submission and would thus be covered by the Safe Harbor." Br. 45. To the contrary: Mr. Wojcik *only* agreed that Dr. Daber made certain statements on the record—Mr. Wojcik did not testify as to the meaning of the message itself. Ex. 5, Wojcik Tr. 187:15-188:7.

Context matters, and Defendants' cherry picking of words does not render Mr. Wojcik's testimony unreliable. Mr. Wojcik's testimony is grounded in the governing test and the specifics of each accused act. That is reliable expert testimony under the Safe Harbor legal requirements and governing authorities. *Amgen*, 944 F.3d at 1339.

5. Dr. Sullivan Properly Considered the Comparable Becton Dickenson-ArcherDX License Agreement

The Becton Dickenson ("BD") license to ArcherDX covers patents related to the use of unique molecular identifiers ("UMIs") or molecular barcodes in library preparation. *See* Ex. 14, Sullivan Rpt. ¶¶ 392-396. Defendants grossly distort the BD license to contend that it is not a comparable license and assert that the royalty rate under the agreement is allegedly [redacted] and not [redacted], as Dr. Sullivan opines. Br. 46. Defendants are incorrect on both counts.

At the outset, Defendants' argument about comparability stands in stark contrast to their response to Natera's Interrogatory No. 4 where Defendants *identified the Becton Dickinson Agreement as a relevant license to the Accused Products.* Ex. 8 at 25. Having admitted relevance, its degree as well as any alleged failure on the part of the expert to address any differences "are factual issues best addressed by cross examination and not by exclusion." *ActiveVideo Networks, Inc. v. Verizon Commc'ns, Inc.,* 694 F.3d 1312, 1333 (Fed. Cir. 2012).

Defendants' inconsistent positions aside, Dr. Sullivan properly assessed whether the BD license involves comparable technology, is economically comparable, and arises under comparable circumstances as the hypothetical negotiation. *See* Ex. 14, Sullivan Rpt. ¶¶ 382-421; *Bio-Rad Labs., Inc., v. 10X Genomics Inc*., 967 F. 3d 1353, 1372-73 (Fed. Cir. 2020) (Assessing a license's comparability requires considering whether the license involves "comparable technology, is economically comparable, and arises under comparable circumstances as the hypothetical negotiation."); *Commonwealth Sci. & Indus. Rsch. Org. v. Cisco Sys., Inc.*, 809 F.3d 1295, 1298, 1303 (Fed. Cir. 2015) (asserted patents "properly valued" with comparable licenses and then adjusted for differences and economics).

Defendants' reliance on Dr. Quackenbush's "limited comparability" opinion is misplaced. Br. 46. Dr. Quackenbush opined that there is "limited comparability" between the BD patents and the Asserted Patents, not that there is no comparability. *See* Ex. 19, Sullivan Reply Rpt. ¶¶ 58-59. Dr. Sullivan explains that Dr. Quackenbush's limited comparability opinion rests on the technologies having a difference in scope, not that the technologies are unrelated, as both sets of patents relate to the library preparation process. *Id.* Indeed, Dr. Sullivan understands from Dr. Quackenbush that, "the technology in the BD patents is sufficiently related to the technology in the patents-in-suit such *that they can be compared*." *Id.* (emphasis added).

Defendants' characterization of the BD license royalty rate is factually wrong. The BD-ArcherDX agreement expressly sets the royalty rate at [redacted] on "Licensed Products." *See* Ex. 2, Sec. 3.2 ("Subject to the terms of this Agreement, Licensee shall pay BD a quarterly royalty of [redacted] on Net Sales of Licensed Products. . ."). The accused roducts covered by the hypothetical license would be "Licensed Products[23]" with the [redacted] royalty the BD agreement defines. S*ee, e.g.*, Ex. 14, Sullivan Rpt. ¶¶ 382-383, 409-410. Defendants' "various adjustments" are to the royalty base—not the royalty rate—and in any event are highly disputed. *See* Ex. 14, Sullivan Rpt. ¶ 385; Ex. 19, Sullivan Reply Rpt. ¶ 64.

Defendants exaggerate Dr. Sullivan's adjustment to the BD licenses [redacted] royalty rate. Dr. Sullivan did not adjust the royalty rate "by nearly a factor of eight…" Br. 46. Dr. Sullivan adjusted the [redacted] rate by a factor of *less than two* and provided detailed reasons for doing so. *See* Ex. 14, Sullivan Rpt. ¶¶ 382-421. Defendants' arguments should be left to cross-examination.

a. Dr. Sullivan Properly Accounted for the Incremental Value of the Patented Use of Molecular Barcodes

Dr. Sullivan analyzed many factors to determine the value of the use of molecular barcodes. Dr. Sullivan relied on Dr. Quackenbush, who explained that the Asserted Patents offer significant benefits over the BD licensed patents, which only concern the use of molecular barcodes in the library preparation process. *See* Ex. 14, Sullivan Rpt. ¶ 396. Dr. Sullivan analyzed several factors, including: (1) the limited roles of molecular barcodes as covered in the Asserted Patents; (2) Defendants' proposal, as a non-infringing alternative, to drop the use of molecular barcodes; (3) ArcherDX's expert report submitted in another litigation asserting that "molecular barcodes do not play a critical role in the accused products" and (4) Natera's history of not licensing its patents.

[23] As opposed to a "Licensed Combination Product." *See* Ex. 14, Sullivan Rpt. ¶ 383.

Id. at ¶¶ 349, 382-421. Dr. Sullivan further established the relatively low value of molecular barcodes (the most basic component covered by the BD license) vis-à-vis product pricing, illustrating that the benefits of the Asserted Patents to the Accused Products outweighs those of the BD patents. *Id.* This complies with Federal Circuit authority. *Bio-Rad Labs, Inc.,* 967 F. 3d at 1372-73; *Commonwealth Sci. & Indus. Rsch. Org.,* 809 F.3d at 1303.

Defendants argue that Dr. Sullivan improperly failed to apportion for the incremental benefit of using molecular barcodes to the Asserted Patents because such use is allegedly in the prior art, including the BD patents. Br. 47. Defendants' assumption is impermissible for purposes of estimating damages—where the analysis is predicated on an assumption of validity and infringement. *Georgia-Pacific Corp. v. United States Plywood Corp.*, 318 F. Supp. 1116, 1122 (S.D.N.Y. 1970), *mod. and aff'd*, 446 F.2d 295 (2d Cir. 1971).[24] Likewise, when a patent claims a novel combination of conventional elements, the proper exercise in assessing damages is not subtracting the value of all conventional elements from the value of the patented invention as a whole; rather, "the question is how much new value is created by the novel combination, beyond the value conferred by the conventional elements alone." *AstraZeneca AB v. Apotex Corp.*, 782 F.3d 1324, 1339 (Fed. Cir. 2015). Dr. Sullivan answered exactly that question and properly attributed the benefits of the claimed novel use of molecular barcodes to the Asserted Patents. *See* Ex. 14, Sullivan Rpt. ¶¶ 382-421.

Defendants' argument is in any event factually disputed. The patented use of molecular barcodes in the Asserted Patents is not the same as the use claimed in the BD patents, or any other

[24] Defendants disagree with Dr. Sullivan's economic comparison of methods with and without molecular barcodes reflected in his report's Attachment J-4. Dr. Sullivan's Reply sharply disputed Defendants' contentions. *See* Ex. 14, Sullivan Reply Rpt. ¶¶ 65-74. Defendants' arguments go to the weight of the testimony, and not to its admissibility.

prior art for that matter. *See, e.g.*, Ex. 16, Spellman Rpt. ¶¶ 98, 104, 109, 119, 137, 141, 144, 149, 150, 159. Defendants' expert, Dr. Cooper, could not identify a single prior art reference that teaches the use of molecular barcodes *in asserted patents' novel combination of steps* claimed. *Id.*

Dr. Sullivan's analysis is not based on a flawed proposition that Defendants would agree to pay twice for the same technology. Br. 47. His analysis properly scales the royalty rate for a less valuable group of patents to reflect the appropriate royalty rate for the separate and more valuable group of asserted patents. *See,* Ex. 14, Sullivan Rpt. ¶¶ 382-421, 503-507. *AstraZeneca AB,* 782 F.3d at 1339 (no need to subtract conventional elements in a novel combination). Dr. Sullivan explains, in detail, how their value is greater than the benefits of the BD patents. *See* Ex. 14, Sullivan Rpt. ¶¶ 395-397. These and other factors that Dr. Sullivan addresses in detail warrant and support the adjusted royalty rate for the hypothetical agreement and are reliable. *Id.*

b. Dr. Sullivan Properly Accounted for the Incremental Value of the Patented Invention to the Success of the Accused Products

Defendants contend that Dr. Sullivan includes benefits from personalization of the accused products in his royalty rate determination. Not so. The ArcherDX presentations relied upon by Dr. Sullivan state nothing about "benefits from the personalization of Archer's accused products," nor do they indicate that personalization, either within ArcherDX's accused products or as a broad technology, improves the limit of detection. *See* Ex. 14, Sullivan Rpt. ¶ 401. Rather, as Dr. Sullivan discusses, the "Personalized Competition" data point, which Defendants incorrectly characterize as an improvement from personalization, refers to the limit of detection of a specific product, Signatera, with no indication that personalization contributes to, let alone is responsible for, its limit of detection. *See* Ex. 14, Sullivan Rpt. ¶¶ 401-403. Indeed, as Dr. Sullivan establishes, it is the accused AMP process itself that drives the limit of detection value and improvement—not personalization. *See, e.g.*, *Id.* ¶¶ 95-117, 382-421; Ex. 19, Sullivan Reply Rpt. ¶ 73. In fact,

Defendants themselves describe how Stratafide, one of the accused products that *does not* require personalization, yields the same, if not better, limit of detection, confirming that personalization *is not the reason* for the improved limit of detection ("Stratafide is based on Anchored Multiplex PCR, a technology [that] demonstrated [sic] 100% sensitivity and 100% specificity. Assays developed based on AMP technology demonstrated Limit of Detection (LOD) as low as [redacted]."). Ex. 19, Sullivan Reply Rpt. ¶ 73; Ex. 18, Quackenbush Reply Rpt. Sec. IV. To the extent Defendants disagree with any of Dr. Sullivan's adjustments, they are free to cross-examine him at trial. The *Daubert* motion should be denied.

III. CONCLUSION

For all these reasons, Natera respectfully requests that the Court deny Defendants' motion for summary judgment and to exclude testimony in its entirety.

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February 11, 2022

CERTIFICATE OF SERVICE

I hereby certify that on February 11, 2022, I caused the foregoing to be electronically filed with the Clerk of the Court using CM/ECF, which will send notification of such filing to all registered participants.

I further certify that I caused copies of the foregoing document to be served on February 11, 2022, upon the following in the manner indicated:

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